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BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

SATURDAY OCTOBER 11 1941

PRINCIPAL CONTENTS

Sulphanilylguanidine for Bacillary Dysentery .. .. p. 497

A Medium Selective for B. dysenteriae (Flexner) 501

A New Sulphonamide 503

Size and Visibility of Virus Bodies 507

Clinical Effects of Tetryl and Trinitrotoluene 509

Leading Articles .. .. .. p. 514

Correspondence 523

Foundation of a Nutrition Society 520

An Ear, Nose and Throat Department in the E.M.S. .. 519

Analysis of a Pain 522

Reviews 512

Epidemiology Section 531

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 11 1941

THE TREATMENT OF BACILLARY (FLEXNER) DYSENTERY WITH SULPHANILYLGUANIDINE

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With a Note on the Preparation of the Drug, by James Walker, Ph.D., D.Phil.

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Search for an efficient intestinal antiseptic has in the past yielded poor results. *In vitro* tests of the bactericidal activity of antiseptics are no guide to their usefulness in suppressing pathogenic bacteria in the gut, for the substance must first pass the acid barrier of the stomach, withstand the action of bile and other intestinal juices, and exert a bactericidal action on the intestinal pathogens in a *milieu* of broken-down organic matter and hordes of saprophytic bacteria. Because the natural intestinal infections of man are so difficult to reproduce experimentally, the bactericidal or bacteriostatic activity of an antiseptic substance on the normal intestinal flora, particularly the coliform group, of experimental animals is probably the most useful index for its therapeutic trial in intestinal infections. Graham (1932) tested in this way a large series of substances which were powerfully bactericidal to the colon bacillus *in vitro*, but he failed to find any which produced an appreciable change in the intestinal flora when given by stomach-tube to mice. With the advent of the sulphonamides a fresh attack was made on the problem, and claims have been advanced for the therapeutic activity of different sulphonamide preparations against intestinal infections mainly on the basis of their bactericidal action on the typhoid-dysentery group of organisms *in vitro* or in the peritoneal cavity of injected animals. Since very large doses of typhoid or dysentery bacilli are usually required to kill a mouse infected intraperitoneally, the animal experiments were little better than tests in the tube. On the clinical side, different drugs, particularly those of the phenol series, have from time to time been popular as intestinal antiseptics. Lately, reports of an apparently beneficial result from the use of sulphapyridine or sulphathiazole on single or small groups of cases of typhoid and dysentery have appeared. As examples, Reitler and Marberg (1941) treated 20 cases of acute bacillary dysentery at Haifa with 1 gramme of sulphapyridine three or four times daily for two to four days, and found that most of the symptoms disappeared in two days' time; while Bell (1941) reported good results in the treatment of 14 cases of Flexner and Sonne dysentery with a total average dosage of 5 grammes of sulphapyridine: in neither group was there an adequate control series. The objections to the use of these drugs as intestinal antiseptics are that they are gastric irritants and readily absorbed from the gut, so that if given in full doses they may not only upset an already irritable stomach but because of the risk of dehydration and oliguria may produce severe toxic effects on the kidneys.

Properties of Sulphanilylguanidine

Marshall and his colleagues at Baltimore conceived the idea of using as intestinal antiseptic a sulphonamide compound which, although soluble in water and efficient chemotherapeutically, was poorly absorbed from the intestine. Of a number of such compounds which they had prepared, sulphanilylguanidine was chosen as being the most active against various bacteria. In 1940 Marshall *et al.* described the preparation of this drug, its pharmacology and toxicity, and its bactericidal or bacteriostatic activity on the intestinal flora of mice; and in a second paper (1941) its therapeutic value was demonstrated in a small series of dysentery infections. In their experience the toxicity of the drug for animals was of the same order as that of sulphapyridine and sulphathiazole, but as only a fraction of sulphanilylguanidine given by mouth was absorbed the risk of toxic effects with it seemed small. What absorption occurred was mainly from the small intestine, so that for a maximum therapeutic effect on the lower bowel infrequent large doses seemed likely to serve best. The absorbed fraction, part of it acetylated, was quickly excreted by the kidneys. Its most remarkable property was its power, when fed to mice, to reduce to scanty numbers the thousands or millions of coliform bacilli in the faeces. For clinical use these authors recommended an initial dose of 0.1 gramme per kg. of body weight followed by a maintenance dose of 0.05 gramme per kg. every four hours until the number of stools daily was four or less; then 0.1 gramme per kg. (0.05 gramme per kg. for adults) every eight hours for another three days. With such dosage they reported good results in 7 cases of acute bacillary dysentery treated within three days of onset; the therapeutic effect was variable in 10 cases treated later in the course of the disease. They quoted Lyon as having obtained excellent results in 15 out of 20 treated cases of severe dysentery, compared with 20 untreated control cases.

The value of a drug which, particularly in wartime, could be used for the control of dysentery was at once apparent to one of us (R. C.), and through the kindness of Sir Henry Dale a supply of sulphanilylguanidine was prepared by Mr. J. Walker, who appends a note on its preparation. Later we were fortunate in obtaining further supplies from

the American Red Cross Harvard Field Hospital through the kindness of Prof. J. E. Gordon and Dr. P. B. Benson, while a generous sample was also given us by Dr. Prescott of the Wellcome Foundation, Ltd.

Material and Methods

Although dysentery was the obvious choice of infection on which to test this new sulphonamide, the prevalent form of dysentery in the community was the usually mild Sonne infection, which, being self-limited and uncomplicated like bacterial food poisoning, did not lend itself to the therapeutic assessment of a new drug. However, with the good will of Dr. W. Allen Daley, Medical Officer of Health to the London County Council, and the sympathetic help of Prof. S. Nevin and Dr. S. A. Mann of the L.C.C. Mental Hospitals Pathological Service, arrangements were made to give the drug a therapeutic trial at Cane Hill Mental Hospital, where, opportunely, an epidemic of Flexner dysentery began in December, 1940, and continued with intermissions until June, 1941. Dysentery in mental hospitals is usually an endemic infection, often flaring up in the winter months and varying in severity from a mild diarrhoea to the most violent dysentery with frequent bloody stools and marked prostration. In this particular outbreak the infection was more severe and protracted than usual. Attempts to control its spread in the early stages by the use of a stock polyvalent Flexner vaccine were unavailing, and the prevalence and clinical severity of the outbreak may have been due to the introduction of a new type of Flexner bacillus along with a large influx of fresh patients. Once introduced into a ward the infection spread quickly to a large proportion of the inmates, who could not easily be taught the principles of personal hygiene. The prevalent type of organism was at first *B. dysenteriae* (Flexner Z) and later *B. dysenteriae* (Flexner X).* The period of our investigation was from January to June, 1941.

All the patients were adults, of whom 130 were under observation. In this report, however, only patients who had both blood and mucus in their stools or who were bacteriologically confirmed to be suffering from Flexner dysentery were accepted for analysis. This reduced the number to 96, of whom 41 were treated with the drug and 55 were untreated controls. Their ages varied from 25 to 76 years; 55 were over 50 and many of them were in poor physical condition; 40 were males and 56 females.

Dosage of Drug.—The drug was given in powder form. It can be introduced as a suspension in water or milk; it has very little taste, and does not produce any nausea or vomiting. At first the prescribed dosage was 6 grammes a day in three doses of 2 grammes for four days, but after a preliminary trial this dosage was changed to 9 grammes a day in three doses of 3 grammes for two days, followed by 4 grammes a day in two doses of 2 grammes. If the diarrhoea was not controlled in four days the maintenance dose of 4 grammes a day was continued for one week. These are smaller doses than those recommended by Marshall *et al.*, but we were anxious to avoid the risk of any toxic effects from a new and clinically untried drug, and this dosage seemed to be therapeutically effective in most cases. However, later experience has convinced us that larger doses can safely be used, and may be advisable in the more severe cases of dysentery. A sample of blood was taken into oxalate twenty-four hours and again four days after starting treatment, in order to estimate the blood level of the drug. A morning specimen of urine was collected on the fourth day of treatment and examined for drug content, protein, crystals, casts, and cellular content. White cell counts were done on a number of treated and untreated cases. Bacteriological methods are discussed later. In all treated cases a liberal supply of fluids was insisted upon during the period of drug therapy, since sulphanilylguanidine, and particularly its acetylated derivative, might have irritative and toxic effects on the kidneys, similar to those produced by sulphapyridine and sulphathiazole, if adequate excretion was not maintained.

Clinical Results

While the principle of the alternate case was adopted in selecting cases for treatment, a fair number of patients did not develop the typical features of dysentery in the first day or two of illness, but were later diagnosed on either clinical or bacteriological findings as Flexner infections. As a result treatment with the drug was reserved for an unduly large proportion of the more severe and classical infections. For purposes of analysis, therefore, the cases, both treated and untreated, were divided into two groups, labelled "severe" and "mild." The criteria of a severe case were a high initial temperature of 101° to 105° F., frequent stools (four to sixteen a day) containing both blood and mucus, and a prostrated toxic patient. The typical course of such a severe untreated case was an abrupt onset with high fever, headache, general malaise, severe abdominal pain, and in a few cases vomiting. Very soon there were frequent stools containing blood and mucus and accompanied by much tenesmus; the patient became quickly dehydrated and was very weak and toxic. Many of these cases had a typical, almost diagnostic, odour. The diarrhoea, usually with blood and mucus, continued for a week or ten days, and sometimes longer, and when the blood and mucus disappeared the motions often remained relaxed for a further few days. The temperature fell by lysis to normal in four to seven days; appetite improved after a week but convalescence was slow and protracted. In the milder case there was an initial rise of temperature to 99° to 102° F., abdominal pain and malaise, and relaxed stools, usually with blood and mucus, for two to five days. The temperature settled fairly quickly; abdominal pain disappeared, but malaise and anorexia persisted for a week or so, and the patient made a slow recovery.

Of 41 treated cases, 28 were classified as severe and 13 as mild; for the 55 untreated cases the distribution was 16 severe and 39 mild. Thus there was a much higher proportion of severe cases in the treated than in the untreated group. Two patients died among the 28 severe treated cases: one, aged 42, on the eighth day of infection despite a dramatic response to drug therapy; the other, aged 62, on the twenty-second day after making a good recovery from his dysentery. Three patients among the 16 severe untreated cases died: one, aged 29, on the third day of infection; one, aged 47, on the seventh day; and one, aged 60, also on the seventh day.

The criteria of clinical response to sulphanilylguanidine were: (1) a change in the character and frequency of the stools; (2) a rapid fall in temperature; and (3) the disappearance of toxic symptoms. A careful daily record was kept of the number and naked-eye appearance of the stools of every patient under observation, particular attention being given to the presence of blood and/or mucus. As the investigation proceeded it was felt that the number of motions a day was a less reliable guide to the response to treatment than the time in days of the disappearance of blood and mucus from the stools. In this connexion the day of disease on which chemotherapy was begun was an important factor in the reckoning. Among the severe cases the average time was 3.0 days from onset, ranging from two to five days, and in this group blood and mucus were present for an average period of 4.8 days, or 1.8 days after treatment was begun. In two patients blood and mucus persisted for more than a week after treatment was started. Among the severe untreated cases the average duration of blood and mucus in the stools was 6.8 days, or exactly two days longer than in the treated series. In the group of mild treated cases chemotherapy was begun at an average of 3.2 days from onset, and blood and mucus were present for 2.8 days from onset, so that in many cases blood and mucus had disappeared before specific treatment was given. The average duration for bloody mucoid stools in the untreated mild group was 2.5 days. This criterion of clinical response was therefore valueless in the mild type of dysentery

Temperature charts of all cases were kept for analysis, but a cursory examination of these showed that the difference in duration of pyrexia between treated and untreated cases was not likely to be statistically significant. The fact that in many cases treatment with the drug was not begun until the third day of illness precluded any striking effect on pyrexia, which in untreated patients was beginning to settle by the third or fourth day of disease. There were, however, outstanding cases with a critical fall of temperature apparently in response to drug therapy, just as there were untreated cases with pyrexia continuing at a fairly high level for five to seven days. It is impossible to say, with the limited numbers under review, whether these were chance occurrences or not.

* We are indebted to the late Dr. W. M. Scott and to Dr. Marion Watson for the final identification of these strains.

The general response and behaviour of an ill patient under treatment with a new remedy is not readily susceptible to analysis, and the evidence must be assessed as objectively as possible by a physician with experience of the disease and with an adequate control series. At first, when the infection was rather mild and the initial dosage small, it was difficult to be positive about the beneficial effect of sulphanilylguanidine. Later, particularly with early treatment of the more severe cases, the clinical response to the drug was very definite and sometimes dramatic. Nursing staff became enthusiastic about its curative value. In a typical severe case improvement of the patient's condition was noted in twenty-four hours after giving the drug, and by the third day the patient was feeling much better with disappearance of toxic symptoms and return of appetite. Bowel movements became much less frequent within two days, though blood and mucus often persisted for three to four days. Most striking of all, convalescence was much shorter than in the untreated cases. In the milder infections, too, the treated patient was quickly sitting up, with good appetite, while the relaxed stools were followed by a period of constipation.

Relapses.—In the untreated series it was not uncommon for relaxed mucoid stools to continue for some time after the patient was clinically well, whereas the treated patient usually became constipated. But in the treated group four of the severe cases and one mild case had slight relapses, with blood and mucus in the stools for one or two days. These fresh attacks all occurred within a week after cessation of drug therapy, and were probably true relapses rather than reinfections. In only one of them was the Flexner bacillus isolated during the relapse.

Bacteriology

In the early stage of this investigation material for bacteriological examination was taken every day of the acute illness direct from the rectum by means of a rectal speculum and stout loop. The material obtained—usually mucus mixed with some faecal matter—was either planted immediately on to plates of MacConkey's medium or emulsified in warm saline and inoculated in the laboratory within one to two hours of taking the specimen. Suspicious colonies were picked next day, inoculated into the appropriate sugars for fermentation reactions, and tested by the slide-agglutination technique with the Flexner I and II polyvalent antisera of the Oxford Standards Laboratory. The results obtained by these methods were not very satisfactory, and towards the end of April a new medium became available which gave a much higher yield of positive results. This medium is a modification of the Difco S.S. formula, which is based on Leifson's (1935) work on the selective inhibitory action of sodium desoxycholate, citrate, and other chemicals on the normal intestinal bacteria. Full details of this desoxycholate-citrate agar and its usefulness in the isolation of the various intestinal pathogens will be published separately by Dr. Martin Hynes. Table I, prepared by Dr. Hynes, shows the results obtained with material from patients with Flexner infections, and demonstrates in particular the value of the new medium in isolating the pathogen during convalescence.

TABLE I.—*A Comparison of the Isolation of B. dysenteriae (Flexner)*

Day of Disease	No. of Specimens			% Positive	
	* McC. + † D.C. +	McC. − D.C. +	McC. − D.C. −	McC.	D.C.
1	16	4	0	80	100
2–4	19	15	1	54	97
5–7	5	10	3	28	83
>7	6	27	82	5	29

* McC. = On MacConkey's medium.
† D.C. = On desoxycholate-citrate agar.

These figures refer to the total number of specimens examined on desoxycholate-citrate agar. So far as the results from individual patients are concerned the Flexner organism was isolated from 59 (61.4%) of the 96 patients in this series. During the period when Hynes's modification of the S.S. medium, or in a small number of cases the S.S. medium itself, was being used, 37 (92.5%) out of 40 patients yielded the Flexner organism; in 6 of these cases neither blood nor mucus was noted in the stools at any time, and others were suffering from mild infections. It is only fair to state that during this period, when additional technical assistance was available in the hospital laboratory, the Flexner bacillus was isolated on MacConkey's medium in specimens from 27 (67.5%) out of 40 patients, which was a considerable improvement on the early results. Latterly specimens of faeces were being used as often as material obtained by the rectal loop and speculum.

Convalescent Carriers

With the new desoxycholate-citrate medium, which detects relatively small numbers of pathogens in the faeces, it became possible to assess the value of sulphanilylguanidine in eliminating Flexner bacilli from the bowel. While it is generally believed that the Flexner organism quickly disappears from the gut after an acute attack, there is little doubt, from epidemiological evidence, that convalescent carriers must exist, and these cases, together with cases of chronic dysentery, are mainly responsible for spreading the disease and for maintaining it as an endemic infection in a community.

If an intestinal antiseptic should prove to be not only beneficial against the acute infection but also able to prevent the convalescent carrier state or the development of chronic dysentery, it would be a great boon to the public health in general and to asylum communities in particular. With the help of the new medium an examination was therefore made for convalescent carriers of Flexner's bacillus in a series of treated and untreated patients, all of whom gave positive cultures in the first week of infection. Among 16 treated cases 3 gave positive cultures after the end of the first week; 2 of these were positive on the eighth or ninth day respectively, and neither of them gave positive specimens after a week's treatment with the drug. The third case had a mild relapse on the tenth day of disease, and gave two positive cultures following this fresh attack, which may have been a true reinfection. In contrast to these findings, among 17 untreated cases 8 were positive after the first week of infection, and 5 of them were still positive in the third week, 2 in the fourth week, and 1 in the sixth week. The difference between the two groups may be expressed in another way. Of 43 specimens of faeces examined from the 16 treated patients after the seventh day of disease, only 4 were positive, whereas 14 out of 54 similar specimens examined from the 17 untreated patients were positive. Thus sulphanilylguanidine given in the acute stage of a Flexner dysentery infection seemed to be effective in preventing the convalescent carrier state. It should be noted, however, that of the eight convalescent carriers in the untreated group three were initially mild infections, and it may be that such cases are more likely to become carriers than those with more acute infections. Our experience with sulphanilylguanidine in the treatment of Sonne dysentery, in which convalescent carriers are common (Cruickshank and Swyer, 1940), suggests that if the drug is given after the diarrhoea has ceased it is less likely to influence the carrier state. As the drug will now encounter much more organic matter and many more saprophytic bacteria in the bowel, larger doses than seem to be effective in the acute diarrhoeal phase may be required to eliminate the pathogens from the intestine of carriers. For the same reason, sulphanilylguanidine may not be an effective prophylactic in a ward outbreak of dysentery.

Absorption and Excretion

It was desirable to find out what proportion of sulphanilylguanidine was being absorbed from the intestine of patients with acute bacillary dysentery and whether it was readily excreted by the kidneys. The concentration of the drug in the blood twenty-four hours and four days after starting treatment and the urinary concentration on the fourth day were therefore estimated on 28 patients by the method of Hynes (1940). In addition an estimate of the total amount of drug excreted in the urine was made in three patients in order to determine more exactly what proportion of the total dosage given by mouth was absorbed and excreted. The average concentration of the drug in the blood, examined about two hours after the last dose of 2 or, more often, 3 grammes and a total amount of 6 to 12 grammes in the previous twenty-four hours, was 1.55 mg. of free sulphanilylguanidine and 2.57 mg. of total drug per 100 c.cm.; on the fourth day, after a dosage of 4 grammes in the previous twenty-four hours, the corresponding blood levels were 0.74 and 1.28 mg. per 100 c.cm. The drug concentra-

tion at twenty-four hours varied for free sulphanilylguanidine from 0.5 to 3 mg. and for total drug from 0.75 to 6 mg. per 100 c.cm.; at four days the corresponding extremes were 0.25 to 1.75 mg. free drug and 0.5 to 2.5 mg. total drug per 100 c.cm. These figures, when compared with the blood levels after similar doses of the other sulphonamides, show that sulphanilylguanidine is poorly absorbed from the bowel and that the amount absorbed bears some relation to the dosage given. The urinary concentration of sulphanilylguanidine on the fourth day after treatment averaged 94.3 mg. per 100 c.cm. for free drug and 150.2 mg. per 100 c.cm. for total drug. The highest concentration, 240 mg. of free drug and 300 mg. of total drug, occurred in the patient who gave the highest blood concentration—namely, 3 and 6 mg. per 100 c.cm. Thus the urinary findings indicated that the absorbed moiety was being readily excreted. The rate of excretion could best be appreciated from the drug concentrations in the measured twelve-hourly collections made on three patients during and immediately after the period of drug therapy. The findings in one of them are given in Table II as an example which was closely paralleled by the other two.

TABLE II.—*The Urinary Excretion of Sulphanilylguanidine after Doses of 9, 9, 4, and 4 Grammes daily from April 12, 1941*

Date	Time	Volume	Sulphanilylguanidine per 100 c.cm.	
			Free	Total
		oz.	mg.	mg.
April 12–13 ..	8 a.m.–8 p.m.	32	30	35
	8 p.m.–8 a.m.	12	170	260
„ 13–14 ..	8 a.m.–8 p.m.	16	120	220
	8 p.m.–8 a.m.	14	150	250
„ 14–15 ..	8 a.m.–8 p.m.	24	60	150
	8 p.m.–8 a.m.	14	110	190
„ 15–16 ..	8 a.m.–8 p.m.	32	70	105
	8 p.m.–8 a.m.	22	110	180
„ 16–17 ..	8 a.m.–8 p.m.	16	60	170
	8 p.m.–8 a.m.	10	100	110
„ 19			10	15

It will be noted that the concentration rose to a maximum between twelve and thirty-six hours after beginning treatment, fell to a lower level on the third and fourth days when the dosage was smaller, and quickly dropped to a very low concentration after treatment was stopped. There is therefore no evidence that the drug is retained in the tissues for any time after absorption. The proportion of acetylated drug varied both in the blood and in the urine between an eighth and a half of the total, and, as with other sulphonamides, there was no clue as to why certain patients conjugate a large proportion and others very little.

In three cases a rough estimate was made of the total amount of drug excreted in the urine during and immediately after the period of treatment. The calculation, based on the total volume of urine and on concentrations of the drug in twelve-hour collections, gave amounts of 7.5, 8.5, and 13 grammes respectively out of a total of 26 grammes ingested by each patient. If these figures represent the actual amount of drug absorbed, then about one-half to two-thirds must remain in the intestine, to be excreted in the faeces. Estimations were made of the drug concentration in twelve specimens, from three different patients, of fluid or semi-solid stools passed during the period of treatment; the concentration varied from 10 mg. (in a very watery specimen) to 700 mg. per 100 c.cm. Actually only half of the specimens gave concentrations above 200 mg. per 100 c.cm., which is the saturation level of the drug. These figures are lower than those quoted by Marshall and his colleagues (1941), and might be regarded as an indication for bigger doses than were used in this investigation.

Toxicity

With the doses used and the small amount of drug absorbed systemic toxic effects such as occur with the other sulphonamides were not anticipated with sulphanilylguanidine. In fact with one exception no clinical evidence of toxicity was noted: a rash of morbilliform type occurred on the twelfth day of treatment in a patient who, because of persistent diarrhoea, had been given a total dosage of 58 grammes of the drug (9 grammes daily for two days and 4 grammes daily for ten days). Marshall *et al.* (1941) commented on the absence of toxic effects in their series of 25 treated children: in a group of 25 adults treated with the drug there were two cases of drug fever and one of mild haemolytic anaemia. The complication that seemed most likely to occur, as a result of the dehydration and diminished urinary excretion, was deposition of the drug in the urinary tract, with consequent irritative or obstructive effects. In no patient in our series, however, was there oliguria or urinary suppression, and no one complained of lumbar pain. Laboratory examination of the fourth-day specimen of urine of 28 patients showed a trace or slight trace of protein in 5: it seemed likely that this finding was related to the infection rather than to the drug. Epithelial cells and leucocytes were seen in about half the specimens, which were all non-catheter; neither red blood cells nor casts (apart from occasional hyaline casts) were noted in any specimen of urine. Crystals, usually in the shape of narrow rectangles, were present in the urinary deposits of 21 out of 28 patients: sometimes scanty, sometimes abundant, the presence and the amount of crystalline deposits bore a close relation to the urinary concentration of the drug. In this series of specimens crystals were usually present when the urinary concentration of free drug was over 100 mg. per 100 c.cm., which seemed odd in view of Marshall's statement that the drug is soluble to 200 mg. per 100 c.cm. Test-tube experiments were therefore made in order to find out the saturation level of the drug in urine of *p*H 5.6. At body heat (37° C.) the solubility was 175 mg. per 100 c.cm., at room temperature (18° C.) 150 mg., and at 4° C. 125 mg. Thus our finding of crystalline deposits with low urinary concentrations of the drug was probably related to the fact that many specimens of urine in this investigation were sent by post to the group laboratory during the winter months; solubility may also be affected by a high level of other inorganic constituents such as would be present in concentrated urine from febrile patients. Where the urinary concentration of the drug was high—as, for example, in the second-day specimens of the patients whose urine was examined daily—sheaves of narrow pointed crystals rather like those of tyrosine were seen in the urinary deposit and were regarded as the crystals of the acetylated drug. Similar crystals were observed in the urine of treated patients not in this series. One of these was a woman aged 86 with a severe *Salmonella reading* infection who was not benefited by large doses of sulphanilylguanidine and who died on the eleventh day of her infection. Histological examination of the kidneys showed marked degeneration of the tubular epithelium but no evidence of any irritative reaction. Nevertheless where large doses of the drug are being given it seems a wise precaution to insist on a liberal fluid intake.

White cell counts were done on 12 treated cases at the end of the period of drug therapy and in 9 untreated control cases. In the treated group the counts varied from 7,900 to 13,000 cells per c.mm., with an average count of 9,666; in the control group the extremes were 7,300 and 14,800 cells per c.mm., with an average of 9,733. Two treated patients with counts of 12,000 at the onset of infection were retested two weeks later and had counts of 9,800 and 10,200 cells per c.mm. respectively, which merely suggests that there is a slight leucocytosis at the onset of an acute dysentery. When it is remembered that more than half of the patients in the series were over 50 years of age, with a natural tendency to impairment of function, it is obvious that sulphanilylguanidine in the doses given has practically no toxicity for the tissues.

Conclusions

Sulphanilylguanidine, a new intestinal antiseptic, has been used in the treatment of 41 adult cases of acute bacillary (Flexner) dysentery with beneficial results, particularly in the more severe infections. A series of 55 cases in the same epidemic served as controls. While a dosage of 3 grammes three times a day for two days followed by 2 grammes twice a day for two to five days was therapeutically effective, larger doses are safely tolerated and may be advisable in severe or refractory infections.

Treatment with the drug in the acute stage of the infection apparently helped to prevent a convalescent carrier state, which was present in about half of a bacteriologically controlled untreated group.

Sulphanilylguanidine probably owes much of its effectiveness as an intestinal antiseptic to its poor absorption from the intestine, since one-half to two-thirds of the drug remains unabsorbed.

Blood and urinary concentrations of the drug were low relative to the dosage given, and toxic effects were conspicuous by their absence. Since crystalline deposits occur in the urine with concentrations over 175 mg. per 100 c.cm., an adequate fluid intake and output should be maintained to avoid local toxicity or irritation in the urinary tract, although there was no evidence of any such effect in this series of treated cases.

The use of a new culture medium, desoxycholate-citrate agar, resulted in the isolation of *B. dysenteriae* (Flexner) from a high proportion of both typical and atypical infections. Its superiority over MacConkey's medium was most noticeable in the isolation of the pathogen during convalescence.

The combination of an efficient intestinal antiseptic and a culture medium which will readily detect mild infections and convalescent carriers may be instrumental in eliminating dysentery from mental hospitals

We wish to thank Dr. G. A. Lilly, medical superintendent of Cane Hill Hospital, for facilities and encouragement throughout this investigation, and the technical staff of the hospital and group laboratories for their help.

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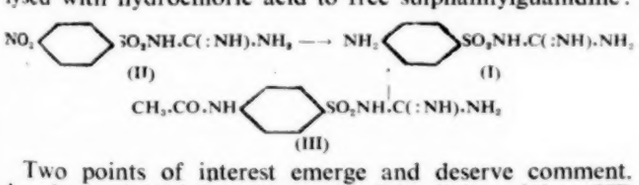
THE PREPARATION OF SULPHANILYLGUANIDINE

It appears that sulphanilylguanidine (I) was first obtained by Buttle *et al.* (1938), who, from its mode of formation, unwittingly ascribed an erroneous constitution to their product (Dewing and Smith, 1941). The compound was first described as such by Roblin and his co-workers (1940), who encountered it accidentally in the course of their study of the synthesis of heterocyclic derivatives of sulphanilamide. These authors, for identification purposes, then obtained the substance by reduction of the nitro group in *p*-nitrobenzenesulphonylguanidine (II), which they synthesized (cf. Winnek, 1940, 1941). A few weeks later Marshall and his colleagues (1940) published a description of a large-scale preparation of sulphanilylguanidine, and their method was followed in the present work. Condensation of acetylsulphanilyl chloride with guanidine nitrate in the presence of a large excess of sodium hydroxide yields acetylsulphanilylguanidine (III), which is subsequently hydrolysed with hydrochloric acid to free sulphanilylguanidine:



Two points of interest emerge and deserve comment. As obtained initially, the acetylsulphanilylguanidine (III) forms a somewhat pasty white solid which tenaciously retains water. Drying is a very slow process under the ordinary conditions (hot oven at 90° C., or vacuum desiccator, etc.), and furnishes apparent yields of the same order as those quoted by Marshall *et al.*—namely, 65 to 70% of theory. Hydrolysis of this product yielded free sulphanilylguanidine also in the amount reported by Marshall *et al.*—namely, 45 to 60% of theory. The process of drying can, however, be greatly accelerated by washing the cake of crude acetyl derivative on the filter with small volumes of spirit and then ether, in which solvents the compound is insoluble. Drying in the hot oven at 90° C. then gives an absolutely dry product in an hour or two, and, on account of the more efficient drying, the yields obtained at this stage appear to be somewhat smaller—namely, 59 to 62% of theory. On the other hand, hydrolysis of the acetyl derivative dried in this way gave free sulphanilylguanidine in the improved amounts of 61 to 72% of theory.

Tests for acute and chronic toxicity of this preparation on mice gave results very similar to those reported by Marshall *et al.* (1940).

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A TELLURITE-IRON-ROSOLIC ACID MEDIUM SELECTIVE FOR B. DYSENTERIAE (FLEXNER)

BY

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AND

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Dysentery bacilli, unlike those of the typhoid-paratyphoid groups, have not shown any peculiar characters enabling the investigator to devise a medium which, while inhibiting the growth of other organisms, allows them to develop and be readily identified.

On litmus lactose agar and on the media of MacConkey, Conradi-Drigalski, and Endo the unrestrained growth of *B. coli* leaves little place on the plates for the development of dysentery bacilli, so that their successful isolation is usually possible only in the early acute stages of the disease and when the stools are planted out within a few hours of their collection. To the antiseptic action of such dyes as malachite green, methyl green, victoria green, brilliant green, fuchsin, crystal violet, and gentian violet dysentery bacilli are more sensitive than most strains of *B. coli* (Churchman, 1912, 1913 ; Krumwiede and Pratt, 1914 ; Kligler, 1918). The new Difco Bacto S S agar specially devised for the isolation of *Salmonella* and *Shigella* strains is designed to meet a long-felt want, a want which may also be satisfied by the medium described in this paper.

The Action of Sodium Tellurite

In the course of an investigation of the suitability of a modified bismuth sulphite medium for the selective growth of Flexner's bacillus, addition of sodium tellurite was found to reduce the growth-inhibitory action both of the bismuth and of the tellurite.

We have shown in the development of our bismuth sulphite medium that the addition of iron salts enabled the *B. typhosus* to develop while the growth of many other organisms continued to be suppressed (Wilson and Blair, 1927). It was this experience which led us to try a combination of tellurite and a ferric iron salt. Having found the bismuth sulphite media unsuitable for use with tellurite, we tried the addition of tellurite to MacConkey's medium, and discovered that the addition of 0.5 c.cm. of a 1% watery solution of sodium tellurite to 100 c.cm. of the medium completely inhibited the growth of nine strains

of *B. lactis aerogenes* and nineteen of twenty-one strains of *B. coli*, whilst all of six strains of Flexner's dysentery bacilli showed some growth, varying from a few isolated colonies to confluent growth. It was clear that tellurite showed possibilities of being used in a medium selective for Flexner bacilli. However, the concentration necessary for the suppression of *B. coli* was sufficient to prevent the growth of all but the most resistant strains of *B. dysenteriae* (Flexner); in other words, instead of hundreds of colonies or a confluent growth, only a few isolated colonies developed. It was then found that the addition of 2 c.cm. of a 4% watery solution of iron citrate scales to 100 c.cm. of the MacConkey tellurite medium allowed a rich growth of the dysentery bacilli and that the suppression of *B. coli* continued. How the iron salt acts, whether by precipitating some of the tellurite or by a process of oxidation, is uncertain. It would seem that the iron salt converts the tellurite into a form which permits rich growth of Flexner bacilli and yet inhibits the growth of *B. coli* to a very large extent. There is an optimum proportion in the ratio of tellurite to iron, and as the result of numerous experiments we found that for 0.5 to 1 c.cm. of a 1% potassium tellurite solution the amount of a 4% watery solution of iron citrate should be 2 c.cm., or of a 4% watery solution of iron alum 1 c.cm. ($K_2SO_4Fe_2(SO_4)_3.24.H_2O$). The basis of our medium is ordinary nutrient agar consisting of distilled water 1,000 c.cm., peptone 10 grammes, Lemco 5 grammes, sodium chloride 5 grammes, powdered agar 20 grammes. The reaction is adjusted to *p*H 7.4. The nutrient agar is sterilized under pressure and is not filtered.

Constituents of the Medium Used

A medium which we employed in many of our experiments, and with which we were successful in isolating Flexner dysentery bacilli from two samples of faeces sent by post, is made as follows:

0.5 gramme of sodium tauroglycocholate and 0.5 gramme of lactose are dissolved in about 10 c.cm. of boiling water in a 100-c.cm. wide-necked flat-bottomed extraction flask; then melted nutrient agar cooled to 60° C. is added up to the 100 c.cm. mark, followed by 0.5 c.cm. of 1% potassium tellurite, 2 c.cm. of 4% iron citrate, and 0.5 c.cm. of 1% neutral red watery solution.

On the surface of this medium colonies of Flexner's bacillus are yellowish, and any strains of *B. coli* that are not suppressed are reddish. In practice we found that stools which show few colonies of *Streptococcus faecalis* on ordinary MacConkey provided abundant tiny colonies on this medium. There was no danger of confusing these colonies and those of Flexner, but it was obvious that their suppression would be a great advantage. After numerous trials of various substances we found that the addition of 0.5 c.cm. of 1% rosolic acid dissolved in absolute alcohol to 100 c.cm. of the tellurite medium secured the desired result. This suppression of *Str. faecalis* by rosolic acid we have confirmed by the examination of over sixty stools and the employment of pure cultures of *Str. faecalis*. Our results confirm those of Bronfenbrenner, Schlesinger, and Soletsky obtained in 1920. These authors found that rosolic acid, or a mixture of rosolic acid and china blue, when added to 100 c.cm. of media to the extent of 0.25 c.cm. of a 2% solution of rosolic acid in 50% alcohol, allowed the growth of colon, typhoid, and dysentery bacilli while suppressing that of Gram-positive bacteria, including *Str. faecalis*.

In our medium the tellurite-iron complex inhibits many coliform organisms, but allows rich growth of Flexner's dysentery bacilli, and the rosolic acid acts not only as an indicator but as an agent for the suppression of *Str. faecalis* and other Gram-positive bacteria. The tellurite-iron-rosolic acid medium is highly selective for Flexner's dysentery bacilli. On this medium the growth of typhoid-paratyphoid bacilli, Sonne's bacillus, and cholera vibrios is completely suppressed, as is that of twenty strains of *Salmonella* food-poisoning organisms kindly supplied to us by Dr. St. John-Brooks from the National Collection; these included such strains as *aertrycke* (mutton), *chester, chaco, berlin, binns, derby, dublin, heidelberg, hirschfeld* para C, *kapsover, kunzendorf, morbificans-bovis, london, limerick, newport, panama, stanley, senftenberg*. The growth of most strains of *B. coli* and *B. lactis aerogenes* is completely inhibited or is very scanty.

In the recent examination of fifty stools we found that heavy inocula of faecal emulsions did not, as on MacConkey plates, lead to confluent growth of *B. coli* but to the formation of discrete colonies, which were sometimes few and sometimes numerous. There was no difficulty in isolating the dysentery bacillus when it was mixed with the faecal emulsion. On the medium few non-lactose-fermenting bacteria developed, apart from Flexner's dysentery bacilli; such as developed have been found to belong to the *Proteus, Alcaligenes,* and *Pyocyaneus* groups, and can be distinguished from dysentery bacilli in that they form pink colonies, larger, more raised, and with a centre more opaque than that of the more translucent colonies of Flexner's bacillus.

Experimental Technique

In our experiments we employed five strains of Flexner's bacillus (V, W, X, Y, Z) obtained from the National Collection of Type Cultures and five strains recently isolated in Northern Ireland. All the strains grew well on the medium which for some time past we have found most satisfactory. It is prepared as follows:

To 100 c.cm. of melted nutrient agar cooled to 60° C. in a flask are added 0.5 c.cm. of 1% rosolic acid dissolved in absolute alcohol, 1 c.cm. of a 4% watery solution of iron alum, and finally 3 c.cm. of a lactose-tellurite solution. The latter solution is made by boiling 20 grammes of lactose in 100 c.cm. of distilled water, cooling the solution, and then dissolving in it 0.2 gramme of potassium tellurite. It is necessary to dissolve the tellurite in the cold, otherwise reduction occurs. This lactose-tellurite solution keeps for weeks, the tellurite being an effective preservative against bacteria, but not against moulds: growth of the latter can be prevented by the addition of 3% of ether and keeping the bottle tightly stoppered.

When the contents of the flask containing the medium have been thoroughly mixed they are poured out into Petri dishes and allowed to set with the lids removed. A large loopful of a thick faecal emulsion in peptone water is spread over the surface of the plate and allowed to dry in the air. After incubation at 37° C. for eighteen hours the pink colonies of Flexner's bacillus are readily distinguished from any yellow colonies of resistant *B. coli* which may have developed. Flexner's bacillus forms alkali and the colony becomes distinctly pinkish red. In most cases the growth can be tested at once on a slide for agglutination with a polyvalent Flexner agglutinating serum. It is also easy to subculture suspicious colonies on to MacConkey's agar and test the agglutinability of the growth. For further proof of the nature of the organism, cultures are made in small test tubes containing mannite and glucose dissolved in peptone water with Andrade's reagent as indicator; the addition to these tubes of agar melted and cooled to 45° C. is a ready method of detecting the absence of gas formation.

When this paper was being completed two stools containing blood and mucus arrived, having been posted the

previous day. Both of these specimens on the tellurite-iron-rosolic acid medium showed hundreds of colonies of Flexner's bacillus and absolutely no *B. coli*, whereas the same emulsion on MacConkey's plates yielded a profuse growth of *B. coli* and no recognizable colonies of *B. dysenteriae*.

Summary

Lactose nutrient agar containing, per 100 c.cm., 0.5 c.cm. of a 1% alcoholic solution of rosolic acid, 0.5 c.cm. of a 1% solution of potassium tellurite, and 1 c.cm. of a 4% solution of iron alum provides a medium on which Flexner's *B. dysenteriae* grows profusely, whereas there is great inhibition of most strains of *B. coli* and *B. lactis aerogenes*. The growth of *Salmonella* food-poisoning organisms, typhoid and paratyphoid bacilli, Sonne's bacillus, and cholera vibrios is suppressed.

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A NEW SULPHONAMIDE
(SULPHONAMIDE E.O.S.)

ITS PHARMACOLOGY, CHEMOTHERAPY, AND CURATIVE VALUE IN MENINGOCOCCAL MENINGITIS

BY

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Although some thousands of sulphonamide derivatives have now been prepared and investigated, very few have displayed any outstanding therapeutic qualities which would justify their general adoption in preference to the simple parent substance sulphanilamide or its popular variant sulphapyridine. The clinician desires something more than an active chemotherapeutic agent. He asks for the means of easy administration to patients of all ages and in all conditions and for freedom from side-actions which are either distressing or dangerous. The new compound employed in this investigation* is freely soluble in water, and 50% w/v solutions are easily obtained. It dissolves to form an almost tasteless preparation with a faintly acid reaction which can be reduced to one of absolute neutrality without precipitation or loss of stability. The treatment of infants and of fastidious, comatose, vomiting, or diarrhoeal patients is therefore easily carried out with solutions given by mouth, nasal tube, rectal tube, or intravenous drip. The familiar 0.5 gramme tablet can be reserved for routine use. In these respects it contrasts favourably with sulphanilamide, which is relatively insoluble in water, with sulphapyridine, which is much more insoluble still, and with sulphapyridine sodium, which, although freely soluble, forms a strongly alkaline solution approximately equivalent in reaction to decinormal caustic soda. Sulphonamide E.O.S. possesses the further attractive feature of low toxicity, and its administration does not lead to the formation of such highly insoluble bodies as the acetylated compounds, which tend to crystallize in the urinary passages when sulphapyridine or sulphathiazole is used (Leedham-Green, 1941).

* The material used in this investigation was supplied by the Research Department of Imperial Chemical Industries Ltd.

Chemistry and Fate in the Body

The substance was first described by Green and Coplans (1940), who identify it as sulphonamide ethyl-alpha-sulphonate,

The side chain was chosen with two deliberate intentions—namely, that of reducing the basicity of the original sulphanilamide and so reducing its toxicity, and that of furnishing a link (as indicated by the arrows) which could easily be broken in the body by hydrolysis, with the liberation of the parent nucleus. In aqueous solution it is stable at room temperature, but hydrolysis occurs on boiling, with the formation of sulphanilamide, acetaldehyde, and sodium bisulphite. Decomposition proceeds more quickly in the presence of acids or alkalis, and is accelerated very greatly indeed by oxidizing reagents such as iodine or hydrogen peroxide. Hydrolysis at body temperature and at *p*H concentrations which are known to occur in the alimentary tract is relatively slow. The pertinent data given in Table I were furnished by the late Prof. A. G. Green.

TABLE I.—*Hydrolysis of Sulphonamide E.O.S.*

Reaction of Solution (2½% E.O.S.)	% E.O.S. hydrolysed in 3 Hours at 37° C.
N/10 HCl (hyperchlorhydria)	4·0
N/20 HCl (normal test-meal peak)	2·8
Neutral	0·7
0·2% $NaHCO_3$	1·8

Throughout this range more than 95% of the drug remains unaffected at the end of three hours, and during this period a large proportion of the drug is absorbed. After absorption hydrolysis proceeds much more rapidly.

A 50% solution w/v was injected intravenously (dose 5 c.cm. =2.5 grammes E.O.S.). Of this only 16% could be recovered unchanged from the urine, and even during the first thirty minutes about one-half was excreted as sulphanilamide or as acetyl-sulphanilamide, the side chain having been removed from the original drug (Table II).

TABLE II.—*Intravenous Administration of Sulphonamide E.O.S. (Man). (Dose, 2.5 grammes in 5 c.cm.)*

Interval after Administration (Hours)	Rate of Urinary Excretion: Unsplit Sulphonamide E.O.S. (Mg. per ½ hour)	Rate of Urinary Excretion: Total Sulphonamide, expressed as Sulphanilamide (Mg. per ½ hour)
0–½	220	471
½–1	140	317
1–1½	40	—
1½–2	10	—
2–5	0	69
5–6	0	115

TABLE III.—*Administration of Sulphonamide E.O.S. by Mouth (Man). Dose, 4 grammes dissolved in water taken between meals at 11 a.m.)*

Interval after Administration	Vol. of Urine (c.cm.)	Rate of Urinary Excretion: Unsplit Sulphonamide E.O.S.	Rate of Urinary Excretion: Free Sulphonamide, expressed as Sulphanilamide (mg. per ½ hour)
0–20 minutes	15	Small amount	Trace
20–45 ,,	15	,, ,,	3·0
45–60 ,,	15	,, ,,	13·4
1–1½ hours	25	,, ,,	15·5
1½–2 ,,	25	None	17·0
2–3 ,,	35	,,	12·0
3–5 ,,	55	,,	11·8
5–7 ,,	50	,,	8·6
7–9½ ,,	60	,,	9·2

The excretion of sulphonamide E.O.S. ceased after two hours, but excretion of considerable amounts of sulphanilamide continued for many hours. The rate of excretion was substantially modified by variations in urinary flow. Excretion was decidedly more rapid during water diuresis. This rapid hydrolysis in the

body can be ascribed provisionally to the presence of oxidizing agents such as tissue oxidases and oxyhaemoglobin.

When a single dose is given by mouth, excretion of unsplit E.O.S. begins within twenty minutes and continues for an hour and a half, after which time E.O.S. can no longer be found in the urine, but sulphanilamide and its acetylated derivative are excreted in substantial amounts throughout the day. The peak rate of total sulphonamide excretion occurs between one and a half and two hours after administration of the drug (Table III). Of the original 4 grammes only about 30 mg. could be found in the urine in its original form. Hydrolysis is therefore almost complete.

With the slower rate of absorption following administration by rectum it was impossible to find any unsplit E.O.S. in the urine, and the peak rate of sulphanilamide excretion was much delayed (Table IV). Nevertheless the drug is therapeutically effective when given in this way (Case 19, Table VIII).

TABLE IV—*Rectal Administration of Sulphonamide E.O.S. (Man). (Dose, 4 grammes in 8 c.cm.)*

Interval after Administration (Hours)	Vol. of Urine (c.cm.)	Rate of Urinary Excretion	
		Unsplit Sulphonamide E.O.S.	Total Sulphonamide expressed as Sulphanilamide (Mg. per ½ hour)
0–½	55	Nil	17
½–1	30	,,	12
1–1½	23	,,	21
1½–2	47	,,	19
2–3	160	,,	26
3–4½	1,150	,,	41
4½–5	230	,,	23

During routine administration of the drug by mouth the unsplit sulphonamide E.O.S. appears in the cerebrospinal fluid (Table V) together with a preponderance of sulphanilamide.

TABLE V.—*Cerebrospinal Fluid (after Administration of Sulphonamide E.O.S. by Mouth)*

Case	Age	Illness	Dose	Lumbar Puncture Performed	Interval between Lumbar Puncture and Most Recent Dose of E.O.S.	Concentration of Drug in C.S.F.	
						Unsplit E.O.S.	Total Sulphonamide, expressed as Sulphanilamide
A	6	Cerebro-spinal meningitis	*Repeated* 2 gm. four-hourly	2nd day	Hours 3¼	Trace	Mg.% 8
				2nd day (later)	4	,,	10
				3rd day	1½	,,	16
B	32	Epilepsy	*Single Dose* 4 gm. fasting		½	Nil	1·6
C	31	,,	,,		1	,,	Trace
D	26	,,	,,		1½	,,	2·6
E	15	,,	,,		2	,,	1·2
F	73	,,	,,		2½	,,	Trace

The analytical methods used were:

Sulphanilamide+E.O.S.=free sulphonamide
Sulphanilamide+E.O.S.+acetylated sulphanilamide =total sulphonamide } Marshall's method (Marshall *et al.*, 1937)

Unsplit sulphonamide E.O.S.:

The following method was devised by A. G. Green: To 25 c.cm. of urine add 5 c.cm. of 10% barium chloride solution and filter. To filtrate add 2 c.cm. of concentrated hydrochloric acid and filter again if necessary. To the clear solution add 1 c.cm. of N/1 sodium nitrite (7.2% solution). If free sulphonamide E.O.S. is present a further turbidity or precipitate will form and can be compared with a standard control.

Conclusions.—Sulphonamide E.O.S. is probably adsorbed unchanged when given by mouth or rectum. In the body it is rapidly hydrolysed, but during therapeutic schemes of routine four-hourly doses small amounts of unsplit drug persist in the cerebrospinal fluid throughout the inter-dose period. When administered orally it is excreted in the urine to a small extent unchanged, but mainly in the form of sulphanilamide with a small proportion of the acetylated derivative of sulphanilamide. On intravenous injection hydrolysis to the extent of 25% occurs within an hour and is complete after two hours. Opportunities for an individual therapeutic action are offered by (1) the production of sulphanilamide *in situ* in the blood and tissues, and possibly in the bacterium itself; (2) the independent action of the unsplit drug; (3) the rapid rate of absorption from the upper alimentary tract and rectum.

Experimental Therapeutics

The toxicity of sulphonamide E.O.S. has been assessed in terms of lethal dose administered to animals by mouth and by clinical survey of phenomena appearing during therapeutic administration in man. Values given by various observers for the toxicity of sulphanilamide measured in terms of L.D.50 range between 60 and 80 mg. for the 20-gramme mouse. Such figures are influenced by the strain of mouse used. In the present research female albinos were employed and parallel doses of sulphanilamide suspension and sulphonamide E.O.S. solution were administered by oesophageal tube. Deaths were recorded seventy-two hours later, when surviving animals appeared to be normal. For sulphanilamide L.D.50 was found to be 70 mg. per 20-gramme mouse. For sulphonamide E.O.S. it was 200 mg., giving a toxicity ratio on a gravimetric basis of about 1:3 in favour of sulphonamide E.O.S. The relative molecular weights of the two substances must be taken into consideration:

$$\frac{\text{Mol. wt. E.O.S.}}{\text{Mol. wt. sulphanilamide}} = \frac{302}{172}\text{; i.e., approximately } \frac{7}{4}$$

7 grammes of E.O.S. are therefore equivalent in nuclear content to 4 grammes of sulphanilamide. Making the appropriate correction, the toxicity ratio becomes 1 : 1.6, showing that the amount of sulphonamide nucleus which can be given in the form of sulphonamide E.O.S. is substantially greater than that which can be given with equal safety in the form of sulphanilamide. Further toxicity tests and an experimental investigation of the curative action of the drug on infected laboratory animals were carried out by Dr. M. Coplans as follows:

(i) *Acute Infections*

Streptococcus pyogenes (from the National Collection of Type Cultures Group A—Griffith No. 5493)

Albino mice, and doses calculated per 20 grammes weight: 5 million streptococci injected intraperitoneally; 1 c.cm. 5% aqueous solution (neutral) E.O.S.=25 mg., given subcutaneously 1/2 hour after inoculation and repeated daily.

21 mice inoculated and treated:
- 3, duration of treatment 2 days. All died on ninth day.
- 18, duration of treatment 10 to 20 days. 11 survived, and cultures taken between 46th and 58th day were all negative.

Controls:
- 18 mice inoculated and not treated. All dead within 17½ hours and organism recovered from heart blood and peritoneal fluid.
- 18 mice treated for 10 to 20 days but not inoculated. 15 survived (3 died on 7th, 18th, and 27th days).

Pneumococcus Type III (from the National Collection of Type Cultures Type III—Griffith No. 2438)

Albino mice, and doses calculated per 20 grammes weight: broth culture (100×M.L.D.) intraperitoneally; 0.5 c.cm. aqueous solution of E.O.S=166 mg., given by mouth 1/2 hour after inoculation and repeated daily.

6 mice inoculated and treated for 5 days. All alive and well 9 weeks later.

Controls:
- 6 mice inoculated and not treated. All dead within 60 hours and organism recovered from heart blood and peritoneal fluid.
- 6 mice treated for 5 days but not inoculated. All alive and well 9 weeks later.

(ii) *Urinary Carriers*

Immature Dutch rabbits were used and the carrier condition induced by Coplans's (1940) method.

B. typhosus:

7 carriers. Treatment started on 19th day. Sulphonamide E.O.S. 2 grammes per kilogramme by mouth alternate days for 5 doses and then daily for a further 33 doses (to surviving animals). In every case the bladder and urine became free from infection.

6 untreated carriers. 1 recovered spontaneously. In 5 infection persisted in the bladder or urine.

B. paratyphosus A:

5 carriers. Treatment started on 40th day. Sulphonamide E.O.S. 2 grammes per kilogramme by mouth daily for 45 doses. In every case the bladder and urine became free from infection

6 untreated carriers. Infection of bladder and urine persisted in all animals.

Conclusions.—Sulphonamide E.O.S. controls acute infections by *Str. pyogenes* and pneumococcus Type III in mice and chronic infections of the urinary carrier type due to *B. typhosus* and *B. paratyphosus* A respectively in rabbits.

Clinical Observations

The clinical data relating to the toxicity of sulphonamide E.O.S. are derived from 130 cases treated for a variety of acute infections. The doses used in different age groups are given in Table VI.

TABLE VI.—*Sulphonamide E.O.S. Dosage (Clinical Toxicity Test) (130 Cases)*

Group	No.	Average Age in Years	Dosage in Grammes					
			Initial		1st 3 days		Total	
			Range	Average	Range	Average	Range	Average
Infants* (up to 12 months)	27	6 12	½–1	0·8	1½–18	10·3	2½–67	21·7
Children (1 to 10 years) ..	31	3½	½–3	1·5	2–45½	19·0	5–82½	36·7
Adolescents (10 to 20 years) ..	17	16	2–4	2·5	12–49	29·3	12–72	44·6
Adults (above 20 years) ..	55	—	1–4½	2·6	9–56½	32·0	15–100	51·9

* The youngest infant, aged 3 weeks, was given an initial dose of 1 gramme, 11½ grammes in three days, and 17½ grammes *in toto*. When first seen she was extremely ill with bronchopneumonia, and artificial respiration was required. An oxygen tent and α-lobeline injections were used. The condition came steadily under control in the course of a few days. No toxic signs attributable to the drug were noted in spite of the exceptionally heavy dosage adopted.

The general malaise of sulphonamide therapy was very little in evidence, and that miserable sequence of pallor, nausea, and vomiting characteristic of sulphapyridine never occurred. In many cases (not included in Table VI) treatment was instituted with sulphapyridine and subsequently completed with sulphonamide E.O.S. The general appearance and subjective feeling of severe illness of these patients disappeared rapidly when the substitution was made. The visible change for the better on E.O.S. therapy was very remarkable indeed.

Cyanosis was commonly seen, but never caused any distress or necessitated the interruption of the prescribed course:

Absent	40%
Trivial	28%
Substantial	29%
Severe	3%
Requiring withdrawal of drug	0%

Vomiting was rarely encountered. In pregnancy and meningitis vomiting often occurs without provocation. If such cases are excluded the trouble was confined to a small minority of infants and young children in whom the causal relation between the drug and the vomiting was by no means clear.

Leucopenia.—Routine blood counts were made without bringing to light any instance of agranulocytosis or simple leucopenia. The leucocytes were never fewer than 6,000 per c.mm. of peripheral blood, with the exception of one case in which the white count fell to 5,400 cells per c.mm.

Anaemia.—Minor degrees of anaemia were found, but not with greater frequency or of greater severity than is usual after severe infective illnesses. No severe anaemia of aplastic or of haemolytic type was ever observed.

Rashes.—One patient developed a simple erythematous rash—a fine pink widely distributed eruption occurring in a young child after a week of treatment with E.O.S.

A curious case of acidosis (Case 25, Table VIII) occurred in a young woman of 28 who was semicomatose from meningococcal meningitis. There were no ketone bodies in the urine, but the alkaline reserve of the blood was low. In terms of CO_2 binding power it varied between 34.8 vols. CO_2% and 36 vols. CO_2% respectively over two successive days (normal value, 53 to 77). The inorganic blood phosphorus remained within normal limits. The *p*H of the urine fell to 5.0 (analyses by Dr. S. J. Hopkins). The outstanding clinical feature was pronounced hyperventilation beginning at the end of the second day of treatment, by which time 40 grammes of sulphonamide E.O.S. had been taken. It persisted for three days, and was unaffected by oxygen administration (B.L.B. mask). There was no cyanosis. Hyperventilation subsided when full doses of alkalis were given. Administration of E.O.S. continued uninterruptedly, and its curative effect as judged by the mental condition, defervescence, and observations in the cerebrospinal fluid was not prejudiced. The temperature was normal within 7 days.

Although the case must be put on record it is by no means certain that the abnormality was caused by the drug, and the complication might possibly have been prevented by a freer use of routine alkalis, always advisable for febrile patients taking sulphonamides.

The general inference to be drawn from these observations is very satisfactory indeed. In spite of the heavy doses given and the cyanosis produced, there were no serious complications, and the assortment of symptoms which distress without endangering the patient when sulphapyridine is used were conspicuously absent.

Chemotherapeutic Effect (Human)

The drug has now been used in a large number of different clinical conditions with apparently excellent effect—e.g., acute *B. coli* infections of the urinary tract, puerperal infection, septic cuts, acute infections of ear, nose, and throat, pneumonia (including pneumococcal and Friedländer infections, the mixed bronchopneumonias of infancy), and septic pleuritic effusions. The expected recovery rate in these disorders is reasonably high even when non-specific therapy alone is carried out. The prognosis varies greatly from case to case. For these reasons it is extremely difficult to secure a datum line from which to judge the success or failure of any new curative method. More trustworthy conclusions can be formed by selecting more intractable diseases, such as chronic *B. coli* infections of the kidney and bladder or purulent meningitis, as the medium for therapeutic assay.

TABLE VII.—*Dosage of Sulphonamide E.O.S. (Acute Cerebrospinal Meningitis—Meningococcal)*

		Adults (Grammes)	Children (Grammes)			
			10 years	5 years	2 years	Infants
1st two doses	6 doses	4	3	2½	1½	1
Remainder of first 2½ days	daily (4-hourly intervals)	3	2½	2	1¼	1
Next 1½ days		2–2½	1–1½	¾–1¼	½–1	½–¾
5th day	5 doses daily (4-hourly intervals); 6th dose omitted during night	1½–2	½–1	½–1	½–¾	½–¾
6th day		1–1½	½–¾	½–¾	½–¾	½
7th day		½–1	0–½	0–½	0–½	½
8th day		0–½	0–½	0–½	0–½	0

Attention has therefore been centred on acute epidemic cerebrospinal meningitis The cases all occurred in the

Guy's Hospital Sector of the E.M.S. during 1940 and the early part of 1941. These patients were suffering from the disease in its acute form and many were very seriously ill indeed. Their ages ranged from 7 months to 63 years. About one-quarter were either less than 1 year or more than 45, and so fell into the age periods of gravest prognosis. The general dosage scheme is given in Table VII. Small variations were introduced to meet the needs of individual cases. The amount of sulphonamide used was not so great as these figures suggest. It must be remembered that 1 gramme of sulphonamide E.O.S. is equivalent chemically to no more than 0.57 gramme of sulphanilamide.

The outstanding clinical features of the cases are indicated in Table VIII. In every instance Gram-negative diplococci were seen in the cerebrospinal fluid. In most cases the organism grew in culture and many of them were typed. The commonest type was Group I, but some were not agglutinated either by Group I or Group II serum.

Case 19 is of particular interest. It demonstrates the efficacy of sulphonamide E.O.S. when administered by rectum. It also indicates that pregnancy does not interfere with the action of the drug and is not affected adversely by it. Normal labour occurred later at full term and the child was correctly formed and well nourished. The mother's health during the later months of pregnancy was excellent and the puerperium passed uneventfully. A considerable number of patients were comatose or semi-comatose on admission. In spite of the high proportion of infants and elderly persons and the coincident pulmonary diseases of Cases 2, 24, 26, and 34, the mortality rate of 9% is reasonably low. Analysis of the factors leading to death in the three fatal cases reveals special features in each case.

Case 1.—This was a neglected case, and chemotherapeutic treatment was not instituted until the third week of illness, when hydrocephalus was already established.

TABLE VIII

Case No.	Age Years	Treatment Day of Illness	C.S.F. (1st Lumbar Puncture) Pressure mm.	Cells (Polymorphs per c.mm.)	Protein Per cent.	Comment	Result
1	7/12	20th				A neglected case in coma with hydrocephalus already established	Died in 48 hours
2	10/12	2nd	300	520	0·24	Intensely ill and unconscious. Had only recovered from pneumonia a month previously	Complete recovery 2½ weeks
3	11/12	14th	+	3,140	0·24	Slow onset. Convulsions just before admission	Complete recovery. Temp. normal in 4 days
4	1 3/12	3rd	+	9,000	0·30	Very severe case. Pneumonia present on admission	Complete recovery. Rapidly controlled, but tardy clearance
5	1 9/12	3rd	+	3,460	0·90	Full average severity. Semi-comatose	Complete recovery
6	1 10/12	3rd	300	1,840	0·10	Average severity	Inadequate initial dosage, recovery protracted but eventually complete
7	1 11/12	2nd	280	4,250	0·45		Complete recovery
8	3	2nd	250	2,140	0.16	" "	" "
9	5	4th	320	7,360	0.10	" "	" "
10	7	5th	290	2,000	0.65	" "	" "
11	7	5th	250	1,620	0.20	Semi-comatose. Old mitral regurgitation. Profuse herpes	" "
12	9	4th	280	3,290	0·38	Average severity	" "
13	13	3rd	230	1,106	0.35	Abrupt onset. Delirium. Screaming. Semi-coma	" "
14	14	2nd	260	4,380	0.29	Average severity	" "
15	16	5th	300	12,700	0.30	Full average severity	Complete recovery. Temp normal in 3 days
16	17	4th	290	7,200	0.25	Average severity	Complete recovery
17	19	4th	240	800	0·20	Full average severity	Complete recovery. Temp. normal in 5 days
18	20	1st	335	2,720	0.36	Semicoma. Petechial rash	Complete recovery
19	22	2nd	250	2,600	0·35	Pregnant, and comatose 5 days. Early medication entirely per rectum. 87 grammes administered in this way over period of 5½ days before patient able to take by mouth. Subsequent progress exceptionally rapid	Complete recovery. Five mths. later gave birth to healthy full-term child
20	24	3rd	200	2,280	0·22	Average severity	Complete recovery. Temp. normal in 4½ days
21	24	3rd	210	3,490	0·31	" "	Complete recovery. Temp. normal in 3 days
22	26	4th	300	10,000	0·50	Insidious onset. Delirious on admission but not comatose	Complete recovery
23	27	3rd	280	8,620	0·37	Full average severity	" "
24	28	2nd	320	19,000	0·56	Very severe case. Coma complete within 24 hours. Fat and difficult to nurse. Vomiting conspicuous. Fluids, food, and drugs by nasal tube	Died on 4th day of treatment. P.M. : meningitis clearing. Cause of death, purulent bronchitis
25	28	3rd	315	28,000	0·52	Very severe, with persistent coma. Hyperventilation and acidosis for several days. Severe facial herpes	Complete recovery. Control established steadily. Temp. normal in 6 days
26	34	6th	324	9,800	0·15	Average severity. Old fibroid phthisis with cavities (X-ray finding)	Complete recovery. Temp. normal in 2½ days
27	35	3rd	280	10,100	0·28	Severe illness. Semicomatose for 2 days, but able to take fluids by mouth	Complete recovery
28	35	2nd	240	7,420	0·10	Average severity	Complete recovery. Terminated by crisis in 36 hours
29	40	4th	350	13,000	0·48	Very severe. Semicoma for several days. Blood transfusion on 5th day of treatment. Temperature normal 36 hours later	Complete recovery
30	46	3rd	320	11,900	0·30	Severe illness; delirium but no coma	" "
31	48	3rd	140+ (Pus too thick to register correctly)	16,000 rising to 84,000	1·50	Intensely ill, comatose, dyspnoeic, cyanosed, and finally hyperpyrexial. Drug administered by rectum	Died after 2 days' treatment. P.M. : suppurative meningitis and acute suppurative pericarditis. Section of heart examined for secondary invaders, but none seen
32	53	4th	210	5,600	0·27	Average severity. Acute monarthritis of rt. wrist, a complication on 2nd day of treatment, continued for a little time after subsidence of fever and cerebral symptoms	Complete recovery
33	56	5th	250	6,200	0·18	Average severity	" "
34	63	2nd	300	9,000	0·90	Severe attack. Semicoma, but able to take fluids by mouth. Acute bronchitis on admission. Bronchopneumonia as a complication after 2 days' treatment, but temp. normal a week later	" "

Case 24.—This patient appears to have died of a complication of the unconscious state, possibly due to inhalation of infected material, rather than from the meningitis itself.

Case 31 acquired a particularly lethal and rare complication—suppurative pericarditis.

There were no deaths among those who were seen during the first week of illness and who remained free from serious secondary infections of the viscera. For these reasons more than for the simple statistical fact of a low mortality rate on a limited series of cases, I feel justified in believing that sulphonamide E.O.S. has a pronounced curative action in this disease. Very diverse figures have been published by other observers using different remedial agents. This diversity is readily understood by anyone who has worked among these patients. The mortality rate is affected greatly by so many factors other than that of the chemotherapeutic potency of the drug employed. It varies with the epidemic, locality, age distribution, the speed with which the diagnosis is made, the amount of medical attention which can be focused on each patient, and, above all, with the perfection of the nursing care available. Superb nursing skill is required by delirious, comatose, or semiconscious patients. I know that I have been particularly fortunate in my house-physicians and nurses.

The figures given below furnish a suitable basis for comparison.

Epidemic 1914-17 (pre-sulphonamide):
5,306 cases; mortality 65%

These national figures were analysed by H. D. Rolleston (1919), who found in them evidence of a dwindling mortality as serum treatment came into more general use.

Present epidemic, first quarter, 1940 (sulphonamides widely used):
4,388 civilian cases; mortality 23.7%

Individual groups of smaller numbers but more unified medical control have yielded better results:

120 cases observed personally by Banks (1940) (sulphapyridine or other sulphonamides used in all cases):
Mortality 10%

154 cases at Wrexham (*Lancet*, 1940) (various doctors) (sulphonamides widely used):
Mortality 12.3%

The mortality in the present series treated with sulphonamide E.O.S.—34 cases (9%)—is therefore closely in accord with the current figures.

Summary

A new sulphonamide of low toxicity and full chemotherapeutic activity in acute cerebrospinal meningitis is described. Less critical clinical data lead one to expect that it will be equally effective in combating infections due to *B. coli* and haemolytic streptococci. More extended clinical observations will probably reveal other fields of utility. In animals it controls acute infections due to *Str. pyogenes* and pneumococcus Type III, and chronic urinary infection by *B. typhosus* and *B. paratyphosus* A. Its low toxicity has been investigated by experiment on mice. The rarity with which in therapeutic dosage it provokes unpleasant side-effects in man has been demonstrated by a clinical survey of 130 cases. It seldom causes vomiting, and malaise attributable to the drug is inconspicuous. It is hydrolysed in the body with the liberation of sulphanilamide *in situ*, and is excreted in forms which are far more soluble than those following the administration of sulphapyridine or sulphathiazole. It possesses the convenient property of ready solubility in water. Neutral and almost tasteless pharmaceutical solutions can easily be prepared for administration by mouth, rectum, or vein.

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THE SIZE AND VISIBILITY OF THE FILTERABLE OR VIRUS BODIES

BY

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The filterable, so-called ultra-microscopic or elementary, bodies, generally spoken of as the viruses, are not easy to examine on account of their very small size and the difficulty of staining them; but fortunately they are nearly always present in enormous numbers, often in almost pure cultures. The measurement of such small bodies is very difficult by eye-piece or screw micrometer, and usually one has to resort to photography.

The Photographic Method of Measurement

Muir and Ritchie (1937) state:

"In the microscopical study of virus particles Barnard has utilized photography by ultra-violet light, which is of shorter wave-length than that of the visible rays, and thus has obtained greater microscopical resolution. By this method he has been able to demonstrate photographically virus particles of 0.075 μ in diameter."

Let us compare this with the results obtainable by the use of the ordinary microscope and objectives in common use when these are employed correctly. The late Mr. Edward Milles Nelson (1909), who devoted the whole of his long life to the microscope and was undoubtedly the greatest authority on the subject, says: "Briefly, the method is to bring the object just to the point of invisibility by reducing the N.A. (numerical aperture), and then the correction for antipoint will be the measure of the object." I might add that one can determine the minimum visible of any objective by the following calculation: for white light of 45,300 waves per inch divide 1.041 by the N.A.; for green light of 50,000 waves per inch divide 0.942 by the N.A. of the objective. A full table of the values of the N.A. is given in Mr. Nelson's paper.

I have used this method of measuring by extinction for many years, employing for this purpose a Leitz 1/10[a] fluorite objective fitted with an iris diaphragm graduated in N.A.s, immediately behind the back lens, and find it remarkably accurate and easy after one has had some practice.

From Nelson's table it will be seen that an objective of N.A. 1.4 will reveal a particle of 0.0744 μ with white light and 0.0673 μ with a green screen. Nelson later, in 1935, informed me that even greater visibility could be obtained by using a motor head-light bulb (3 amps 12 volts with a transformer, as suggested by Ivimey-Cook), with the filament in focus, and a deep blue screen. Then the size of an object seen would be 0.841 divided by the N.A.; so that an objective of N.A. 1.3 would show a particle 0.065 μ, and one of N.A. 1.4 a particle 0.06 μ, in diameter. From these figures, given in much greater detail in a previous paper (Coles, 1929), ultra-violet microscopy does not seem very urgently needed.

Mr. Eliot Merlin (1929), the distinguished microscopist, in concluding his masterly article, says:

"In the writer's opinion it is of paramount importance that the true optical capacity of the ordinary worker's microscope, furnished with ordinary glass and fluorite achromatic or apochromatic object-glasses, should be clearly understood and not underestimated, this being the tool exclusively used by thousands of laboratory and technical workers all the world over. It cannot be too emphatically maintained that it is an experimentally absolute fact that an object-glass of 0.4 N.A. (i.e., a common

1/2-inch) will, in white light of wave-length of 45,300 per inch, just render visible a particle of 0.262 μ in diameter; and similarly the 1/12 oil immersion of 1.30 N.A. in common laboratory use should, if properly used to its full defining capacity, reveal particles of not less than 0.08 μ diameter in white light, of 0.0724 μ diameter with a screen wave-length of 50,000 per inch, and of 0.057 μ with the photographic wave-length of 63,500 per inch."

Stained Films and Filtration Method Compared

In recent times organic membranes such as collodion have been devised by Elford (1931) to test filterability. These are called "gradocol" membrane, and by their means Elford and his co-workers have computed the size of the particles. A list of filterable viruses, with their size, is given by Mackie and McCartney (1938). The unit used to express these minute viruses is mμ—i.e., one-thousandth part of a micron (μ) or one-millionth part of a millimetre.

When we compare the size of the filterable viruses as determined by microscopical methods on stained films we are at once struck with the extraordinary difference between these and those obtained by filtration methods. The following measurements of the elementary bodies of definite virus diseases will show how much the results differ.

The size of the virus of *variola* and of *vaccinia* as determined by filtration is stated to be 0.15 to 0.175 μ. They were not recognized as the causal organisms till Paschen described them in 1906, but as a matter of fact Dr. John Buist of Edinburgh had fully described and photographed them nearly twenty years previously. Buist (1887), after staining them with aniline gentian violet, gave their size as from 0.15 to 0.5 μ; and von Prowazek (1912) gives exactly the same figures. Mr. Nelson and Mr. Eliot Merlin, knowing nothing of these figures, estimated the size of some of them as up to 0.45 μ in preparations stained with Giemsa which I sent them in 1922. Vaccinia was the first of the filterable bodies that I dealt with in my work on the viruses in 1913.

The size of the virus of *foot-and-mouth disease* is given as 0.01 to 0.02 μ, or 10 to 20 mμ, and it is regarded as one of the smallest of filterable bodies and quite invisible.

In 1929 Sir Charles Martin, then director of the Lister Institute, kindly sent me films from the vesicles of cases of foot-and-mouth disease, and later sealed ampoules of the filtrate; and in 1933 Dr. (since Sir) John Ledingham, his successor, sent some of the filtrate—both through the kind service of Dr. J. T. Edwards. Films made from the filtrate were fixed in alcohol and stained for twenty-four to forty-eight hours in well-diluted Giemsa. Films were also made with indian ink as in Burri's method, and control films of the ink alone were made at the same time. Lastly, the filtrate was spread in thin film on perfectly clean slides and merely allowed to dry in the air. When these were quite dry they were put under a cover-glass and the margins sealed with cement, taking great care that none of the cement should run in—i.e., they were mounted, unfixed, and unstained in air. It is interesting to note that these preparations and the indian-ink films mounted in 1929 and 1933 are to-day in as good condition as when they were made.

The Giemsa-stained films, when examined with the 1/10-inch oil-immersion objective, show clearly innumerable very fine virus bodies, differing from those seen in other virus diseases, such as vaccinia, herpes, molluscum, etc., on which I have been working for the last twenty-eight years, only by their enormous number and their small size. These stained preparations, when examined by dark-ground with only the 8-mm. or 1/3-inch apo-objective and an 18 compensating ocular, show the minute bodies exceedingly well. The indian-ink preparations under the oil-immersion objective reveal the elementary bodies very distinctly, in marked contrast to the control film of ink. The merely air-dried unstained films mounted in air, when examined by dry dark-ground illumination with the same objective, distinctly show the minute bodies, and exclude the possibility of their being colloidal protein molecules or precipitates from the stain.

Mr. Eliot Merlin, who has during the past years examined nearly all my preparations of virus bodies of various diseases, writing in 1929, confirms my findings in every way. He describes the preparations of foot-and-mouth disease as consisting of densely packed strongly stained particles, measuring from 0.15 to 0.3 μ in the stained films, and precisely similar bodies were seen in the indian-ink slides. He says:

"Your findings *re* size and appearance are in agreement with the facts as they appear to me, and the presence of the bodies in the unstained, merely air-dried, films is pretty conclusive that what we had seen in the stained films was not due to stain debris. The foot-and-mouth virus seems to me to greatly resemble the vaccine and many other virus bodies which we have examined previously. What surprises me is that the bodies with which the films swarm should be considered difficult to define with the ordinary microscope. I think the appearance of the bodies under the microscope is in itself fairly convincing to anyone with an open mind on the subject. If they be not virus bodies one wonders how they can be proved not to be."

Causal Virus of Various Diseases

The causal virus of *yellow fever* is said to be one of the smallest of the elementary bodies, and according to filtration experiments is estimated to measure 0.018 to 0.027 μ, or 18 to 27 mμ. Blood films from monkeys infected with yellow fever were kindly sent me by Prof. Edward Hindle in 1929 and Prof. W. Schüffner in 1931, and when these were stained with Giemsa I found minute bodies in the red blood corpuscles and also free in the plasma. They varied considerably in size; many measured from 0.1 to 0.35μ, but some were only just visible specks. The larger bodies were resolvable in most cases into three or four minute spots not larger than 0.1 μ. The number seen varied according to the day of the disease; they were most numerous on the second or third day of the fever, and in several of the films many free and intracorpuscular forms could be seen in every field.

In blood films of patients naturally affected and in volunteers inoculated with about 0.33 c.cm. of dried serum of infected blood from cases of *dengue fever*, somewhat similar bodies were found. These were numerous on the first three days of fever, considerably less numerous on the fourth day, and on the fifth and sixth days they were exceedingly few, being found only with difficulty. Blood films from three cases of *sandfly* or *pappataci fever* taken during the first twenty-four hours showed bodies almost exactly like those of dengue. Mr. Merlin kindly examined and confirmed my findings in these three virus diseases, which have been described in detail with photomicrographs elsewhere (Coles, 1937).

Lastly, let us examine another of the extremely small virus bodies, that of *poliomyelitis*, which measures according to filtration experiments 0.008 to 0.017 μ, and according to other textbooks from 0.010 to 0.020 μ. I have received air-dried films from proved infective filtrate of poliomyelitic monkey-cord suspension from three reliable sources—namely, Dr. J. A. Kolmer, Dr. A. B. Sabine, and Dr. E. W. Schultz, all of the U.S.A.—and after staining these in Giemsa very definite elementary bodies were easily seen. They varied in size from 0.15 to an average of 0.2 to 0.3 μ. These have been described and photographed (Coles, 1939).

Discussion

How can the marked difference in size of the elementary bodies as determined by filtration experiments and microscopical methods be explained? It should be remembered that the size of the virus particles as measured by means of collodion filters represents the size of the *smallest* of the *living* bodies and not that of the average of the stained elementary bodies. Have fixation and staining any effect on the size of the particles? The answer to this is strikingly in the affirmative, and to a much greater extent than most of us realize. In 1929 I stained a film containing *Treponema pallidum* in Giemsa for fifteen to twenty minutes, and after washing and drying examined it with the 8-mm. or 1/3-inch apo-objective by dry dark-ground illumination, without any cover-glass or mounting medium. A spirochaete was very easily found by this means, partly because the eosin red of the Giemsa shows up brilliantly by dark-ground illumination, but chiefly because the difference in its refractive index and that of air is so great. The position of the spirochaete was logged, and ringed with the marker. The oil-immersion objective was then turned on, and the spirochaete was practically invisible; only after prolonged careful search was it seen, and it appeared as the very thinnest and finest spirochaete possible. The slide was placed back in the stain for twenty-four hours, and then it was markedly thicker and very easily seen with the oil objective. A film or a section stained by any of the flagella stains after mordanting, or in silver-impregnated preparations, shows spirochaetes and leptospira as very thick coarse structures, easily seen with quite low-powered objectives.

As the virus bodies are probably very minute organisms, why should the difficulty of examining them be further increased by restricting the examination to them in the living condition? Do we examine sputum for tubercle bacilli, or the diphtheritic membrane or its cultures for the bacilli, in the living unstained preparations? The size of all bacteria is determined in stained preparations, and in the case of the tubercle bacillus in films mordanted by carbolic acid and heat. The size of the tubercle bacillus is generally given as varying from 2.5 to 3.5 μ in length and 0.3 μ in thickness: has anyone detected this bacillus in its unstained living condition, and can anyone even guess at its size in its living state?

The only reason I can imagine why the elementary bodies are studied in their living unstained state is that the very few exponents of ultra-microscopy would have us believe that this is the only correct method: even if this method were adopted the viruses would never be seen but could only be photographed.

Conclusions

I am of the considered opinion (*a*) that all the filterable virus bodies, including the smallest and the so-called invisible virus of foot-and-mouth disease and that of infantile paralysis, are easily within the range of the ordinary microscope when used correctly; (*b*) that ultra-microscopical methods are not essential, and their use has so far added little to our knowledge.

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CLINICAL MANIFESTATIONS OF TETRYL AND TRINITROTOLUENE

BY

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AND

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Since many filling factories have been built recently in different parts of the country it might be of interest to practitioners to know something about the effects on the human body of continued exposure to tetryl and trinitrotoluene.

Tetryl, or "C.E."

This compound is a sharp crystalline powder, yellow in colour. Its clinical manifestations are as follows:

1. The powder stains the skin of the hands, face, neck, and also the hair, and this colour deepens to orange on exposure to sunlight. It should be emphasized that the staining varies considerably in different workers and bears no relation whatever to any of the following manifestations.

2. New workers sometimes complain of a sharp tingling sensation in the nose. This causes sneezing and more rarely epistaxis, and is due to the irritating effect of the crystals on the nasal mucous membrane.

3. The commonest complaint from tetryl workers is dermatitis. This starts as an erythema, followed by a papular eruption accompanied by some exfoliation. It arises in the region of the sweat glands of the face—i.e., the naso-labial fold and submandibular regions of the neck. It may spread all over the face, causing severe irritation, and in some cases gross oedema of the eyelids, which may prevent the patient opening the eyes for two or three days. In severe cases secondary sensitization may occur on the hands, arms, and trunk. Should tetryl come into contact with the conjunctivae a mild conjunctivitis results. Constitutional symptoms are present only in the more severe cases, usually as headaches and general malaise. They are to some extent understandable, as patients suffering from extensive rash often lose sleep. The treatment of C.E. dermatitis is first and foremost removal from contact with the powder. It is not enough merely to change the worker's occupation; he or she must be removed right away from the vicinity of the powder, otherwise the condition will be aggravated by the small amount of dust present in the atmosphere in all shops where tetryl processes are carried on. It is also important that the worker be given a complete change of working clothes. The local treatment, generally successful, consists in frequent applications of calamine lotion or, if there is much desquamation and drying of the skin, lotio calaminae oleosum. A word of warning is, however, necessary when using the latter preparation: tetryl workers should be told on no account to use oily preparations on their skin as a preventive measure, as by so doing ideal conditions are produced for the development of a second attack of C.E. dermatitis. Mild cases clear up in a few days, but severe rashes often persist for two or three weeks. Suspension from work is seldom necessary. When the dermatitis has quite cleared up the worker may return to contact work, but if a second or third attack occurs it is an indication that the patient is very susceptible and should be removed permanently from tetryl work. In our experience those workers who develop oedema of the face and periorbital tissues are bad risks, and we remove them permanently from contact at the first outbreak of the rash.

4. Although it is not generally admitted that tetryl gives rise to any constitutional symptoms, we have found that numbers of new workers complain of epigastric pain, with nausea or vomiting. These symptoms, like those of T.N.T. toxic gastritis, bear no relation to food and are seldom severe enough to keep the patients away from work. Such workers are removed from contact until the symptoms abate. They are then allowed to return, and usually no further trouble arises.

Trinitrotoluene, or T.N.T.

T.N.T. is a yellowish crystalline powder more stable than C.E. and is used either by itself or mixed with other sub-

stances—e.g., ammonium nitrate (amatol), barium nitrate (baratol). It is a highly toxic substance, of which the clinical manifestations are as follows:

1. The hands and, more rarely, the face and the hair are stained orange, but the staining is not so deep as with C.E. This staining should not be confused with the yellowish coloration due to jaundice.

2. *Dermatitis.*—This arises on those skin surfaces which are exposed to direct contact with the explosive—i.e., hands, forearms, neck, wrists, and ankles, the last three areas through friction from the operator's clothing. It seldom appears on the face, but this may be involved in a general outbreak all over the body. On the hands it starts as a sago-grain eruption, and is particularly evident between the fingers and on the thenar eminence. Elsewhere it takes the form of a coalescing papular eruption with areas of erythema. Desquamation is the rule, and may be severe, leading to complete exfoliation of the hands and feet. Small "powder"-holes are also seen. The irritation is intense; and treatment is the same as for C.E. dermatitis—i.e., removal from contact and local application of bland lotions and ointments. One attack of T.N.T. dermatitis, unless unusually severe, is no bar to further employment with the explosive.

3. *Cyanosis.*—T.N.T. exerts a specific action on the haemoglobin, forming a mixture of methaemoglobin and NO-haemoglobin. A large percentage of these workers are "cyanosed" to a greater or lesser degree and present a typical appearance. The lips, tongue, and mucous membranes become a greyish-mauve shade, very different from the true cyanosis of cardiac or lung disease. There is no real anaemia, and very often the condition is symptomless. In fact, we have met workers looking quite purple who declare that they have never felt better in their lives. When present the symptoms are those of oxygen dearth—i.e., fatigue, lassitude, and dyspnoea on exertion. At one time it was our practice to remove from T.N.T. contact all workers showing this sign no matter to what degree, but now we allow mild cases, in which the patients are otherwise well, to remain in contact under observation.

4. *Toxic Gastritis.*—This is a definite syndrome, and is not to be confused with other forms of gastritis arising in T.N.T. workers, including latent hypochlorhydria, which may be unmasked by the action of the trinitrotoluene. The symptoms are: (1) central epigastric pain of a colicky nature, relieved by rest but not by vomiting, and bearing no relation to food; (2) nausea with or without vomiting; (3) a feeling of tightness in the chest; (4) anorexia; and (5) constipation. The cardinal symptom is pain. These patients present a distinct appearance. Cyanosis may or may not be present, but they show a greyness of the face, with a worried expression, and often a definite pallor over the bridge of the nose extending on to the cheeks: the tongue is usually clean. Examination of the abdomen reveals nothing except slight epigastric tenderness, probably due to the constant retching and vomiting. The treatment again is immediate removal from all contact, including the changing of any contaminated clothing and a thorough cleansing of the skin. In very early cases the patient need not be suspended from work, but if there is much vomiting—in our opinion the most important symptom—rest in bed is indicated, combined with saline purges and a high carbohydrate diet containing plenty of fresh fruit and vegetables. There is some evidence to show that vitamin C in large doses may be of value in these cases. Workers who have had a severe attack of toxic gastritis should not be allowed to return to T.N.T. work.

5. *Toxic Jaundice.*—Fortunately this is a rare complication, but it carries a 30% mortality, and all such cases must be treated as serious. It may be heralded by an attack of cyanosis or toxic gastritis, or it may arise *de novo*, patients being found who are symptomless and maintain that they feel perfectly well. The jaundice starts in the conjunctivae and spreads rapidly to the skin. It is a late and grave sign, and indicates severe liver damage. These patients should always be removed to hospital, as it is impossible to carry out adequate treatment at home. The treatment is the same as that for toxic jaundice due to other causes. On admission to hospital the patient should be given a warm bath, and if possible the skin should be scrubbed with acetone or ether to remove any trace of T.N.T. that may still be present. Special attention should be paid to the hands, nails, and hair. Cyanosis may be treated with inhalation of oxygen and carbon dioxide, but this is only necessary where there are definite symptoms of oxygen dearth. The bowels should be kept open by saline purges, and the diet should contain fresh fruit and vegetables, and be rich in carbohydrate, calcium, and vitamin C. It has been maintained that Webster's urinary test for T.N.T. is invariably negative in cases of toxic jaundice, but we are of the opinion that this is not so. We have obtained a positive reaction in a severe case six weeks after admission to hospital. Prognosis on these cases is difficult and should be given with great caution until the patient is well on the way to recovery and the jaundice has cleared up. It is often months before they are fit to return to work, and on no account should any patient ever be allowed back on T.N.T.

6. *Aplastic Anaemia.*—This is a still rarer complication, nearly always fatal and sometimes preceded by jaundice. We have seen three cases, all of them fatal, but in only one was there a definite history of jaundice.

Conclusion

These manifestations appear formidable on paper, but the percentage of workers in contact who are affected is small. Our experience points to the fact that, other things being equal, personal idiosyncrasy must play an important part in the production of toxic symptoms. We are sure that factory medical officers as a body would willingly co-operate with general practitioners in helping to diagnose these somewhat unusual conditions.

Medical Memoranda

Preliminary Note on the Properties of s-Methyl Isothiourea Sulphate

While working with some thiourea derivatives it was observed that s-methyl isothiourea sulphate when administered intravenously in animals raised blood pressure and stimulated respiration. Further observations showed that it also acts when given by mouth. The pharmacological properties of the substance have apparently not been described hitherto, and are manifest in doses which after repeated trials appear to be harmless in lower animals and in man. The circulatory effects have been observed in the dog, cat, rabbit, and man. The rise of blood pressure is either mainly or entirely of peripheral origin, since it takes place after destruction of the central nervous system. The blood-pressure increase is not likely to be the result of stimulation of sympathetic-nerve endings, as it occurs when these endings are paralysed by ergotoxine.

Other smooth muscle besides that of the blood vessels is contracted by s-methyl isothiourea sulphate, notably plain muscle of the isolated intestine. In the whole animal, however, this action on the intestine is not a prominent feature except with big doses. A more detailed communication describing the action in animals will be published shortly, in collaboration with Dr. M. McGeorge (Dunedin) and Prof. Mahomed Sherif (Cairo).

Following animal investigations it was decided to study the action in man. The work in this connexion began in collaboration with Dr. Nassif in Cairo and has been continued by me. It has been shown in healthy men that doses of 0.2 to 0.4 gramme of s-methyl isothiourea sulphate when taken orally cause slowing of the heart and usually a blood-pressure rise. No subjective sensations have been observed to accompany these changes. Two doses of 0.4 gramme given with an interval of about thirty minutes between them have been administered on a number of occasions without leading to subjective sensations. The fall in heart rate is then as much as 20 beats per minute, and in some instances the heart rate has dropped to below 50. On several occasions healthy volunteers carried out a standard Army exercise-tolerance test before and after administration of

s-methyl isothiourea sulphate and observed no special difference as a consequence of taking the substance.

Its Possible Value in Cases of Shock

Some observations have been made by me in man and in experimental animals to ascertain if this substance might be of value in the treatment of surgical shock. It has been noted in about twenty obviously moribund patients, mostly medical cases with terminal circulatory collapse, that the systolic blood pressure may rise promptly from, say, 60 to 120 mm. after the intravenous administration of 0.2 to 0.4 gramme. The diastolic pressure is raised proportionally. The blood pressure remains elevated for fifteen minutes to one hour. The heart rate, however, may fail to slow or does not diminish to the degree observed in health. Some of these results were encouraging in that several moribund patients made a temporary recovery. Two cases of severe surgical shock were treated by the intravenous injection of s-methyl isothiourea sulphate. Both patients survived, and improvement coincided with the administration of the substance. It is regretted that most of the clinical observations were not made on cases of surgical shock, but opportunities for a satisfactory study of this subject are lacking in New Zealand.

More definite evidence has been obtained that the substance is of value in treating acute shock produced experimentally in healthy animals. Thus crushing of limbs and extensive abdominal injuries were employed in anaesthetized cats and dogs to reduce the level of the blood pressure to 30 or even 20 mm. Hg. Ordinarily when the blood pressure has been reduced to such levels cessation of the heart beat usually follows within a minute or two. A majority of animals with blood pressures of 20 or 30 mm. Hg were revived for periods of one or more hours when treated with s-methyl isothiourea sulphate intravenously. It seems, therefore, that the substance delays death if given to animals in extreme traumatic shock. There is thus a chance that the substance would be useful to tide over air-raid casualties which cannot be removed to a place with facilities for transfusion.

The substance also may be worthy of clinical trial in those cases of traumatic shock in which a vasoconstrictor substance could be of value, but even so it should be regarded as an adjuvant and not as an alternative to methods of treatment which restore the blood volume. Patients whose blood pressures remain at a low level despite restoration of the blood volume might be benefited by s-methyl isothiourea sulphate.

In my patients dosage has been controlled by observing the pulse and blood pressure. It appears that in divided doses as much as 1 to 1.5 grammes may be administered in the course of three hours, and probably more would be tolerated. Solutions have been sterilized by tyndallization and kept in ampoules, 0.2 gramme in 2 c.cm. So far only one contraindication to the use of this substance has been found—namely, that it should not be employed in congestive heart failure.

F. H. Smirk, M.D., F.R.C.P.,
Professor of Medicine, University of New Zealand, Dunedin.

Malachite in the Control of Bilharzia

The possibility of controlling bilharzia in Southern Rhodesia has been under investigation for the past two years. This work was begun at the instigation of the medical director of Southern Rhodesia, Dr. A. P. Martin, with the aid of a grant from the trustees of the State lottery. I proceeded to the colony in the first place in company with Sir Malcolm Watson, director of the Ross Institute of Tropical Hygiene. Certain results of this work seem to be important enough to merit immediate announcement.

An essential phase of the investigation has been a search for effective and practical means of destroying the intermediary hosts of human bilharzia—namely, the snails *Physopsis globosa* and *Biomphalaria pfeifferi*. Previous attempts to destroy these dangerous snails have centred largely around the use of copper sulphate. The principal objections to the use of this substance are its relative toxicity to man and other mammals, its great solubility (approximately ten parts of copper per hundred), and its high cost. Copper carbonate is at least as lethal to snails as is copper sulphate, it is much less soluble than the sulphate (approximately one part of copper per million), and in saturated solution it has been proved by experiment in Southern Rhodesia to be non-toxic to white rats when given in repeated doses. The relatively high cost of copper carbonate as well as of the sulphate has led to a search for some less expensive form that would be suitable for control work on a large scale.

Malachite (mineralized basic copper carbonate) when ground fine enough to pass through a 200-mesh sieve has been found to be suitable for this purpose. In this condition malachite from two sources in Southern Rhodesia has been proved to be effective in destroying snails both in the laboratory and in actual bilharzial pools in the field. The present cost of malachite in many parts of Africa is less than £1 a ton. Finely powdered malachite yields an effective concentration (dissolved and colloidal) of 0.5 part of copper per million when placed in natural water (from the Macabuzi River, near Salisbury, S.R.). It has been found that the solubility of this substance is considerably increased by mixing it with fresh brewer's waste (i.e., fermented barley) or with the powdered pods of a common Rhodesian tree, *Swartzia madagascariensis*.

These methods of destroying snails will play an important part in a campaign for the control of bilharzia in Southern Rhodesia which will begin shortly. A full account of the control methods to be used is in preparation.

I am grateful to the Medical Director of Southern Rhodesia for permission to publish this note.

Salisbury, Southern Rhodesia. Alan Mozley, D.Sc Ed.

Melanotic Carcinoma: Sudden Spread after Hysterectomy

The following case may be interesting enough to be worth recording.

Case Report

The patient, aged 41, had hysterectomy performed for fibroids of the uterus on April 25, 1941. Her only complaint was menorrhagia. At operation a routine inspection of the abdominal contents revealed no other abnormality. Pre- and post-operative examination of the chest showed no disease, and the patient left hospital after a normal convalescence. The pathological report on the uterus indicated simple myoma only.

The patient was readmitted on August 1 complaining of abdominal swelling and vomiting for two weeks; for one week she had been breathless. Symptoms had come on quite suddenly twelve weeks after operation. On admission she was cyanosed and breathless at rest; there were scattered subcutaneous black nodules, including three in the abdominal scar; the abdomen was distended with fluid, but a large nodular liver was readily palpated. Search for a primary melanoma revealed only a small scar over the left clavicle. The patient then gave a history that five years ago she had had a "black naevus" there. It was treated with carbon dioxide snow, but increased in size—whereupon it was excised under local anaesthesia. There had been no recurrence since.

She died on August 7. At necropsy melanotic carcinomatous deposits were found in almost every organ of the body—heart, thyroid, lungs, meninges, and brain. The liver weighed 110 oz., and there were profuse deposits in the mesentery, kidneys, spleen, suprarenals, pancreas, and stomach. The abdominal scar was studded with melanotic deposits. The urine gave a positive test for melanogen.

Twelve weeks previously there had been no macroscopical abdominal deposits. If the sudden spread of melanotic deposits was purely coincidental the rapid dissemination after five years' complete quiescence is noteworthy. It is, however, interesting to speculate whether the operation on a distant site initiated the spread; whether, in fact, the malignant cells had lain dormant for five years only to be stirred into activity by the mechanical or physiological disturbance of the operation. Although so far as I know no mechanism for this is described, it seems to be a more possible explanation.

My thanks are due to Mr. Edgar Freshman, under whom the case was admitted, for permission to report it, and to Dr. Norman Ashton, who carried out the necropsy, for the use of his report.

Kent and Canterbury Hospital. Leslie J. Temple, F.R.C.S.

Reviews

EVACUATED CHILDREN

The Cambridge Evacuation Survey. A Wartime Study in Social Welfare and Education. Edited by Susan Isaacs, with the co-operation of Sibyl Clement Brown and Robert H. Thouless. (Pp. 231. 8s. 6d. net.) London: Methuen and Co., Ltd. 1941.

So much feeling has been aroused by the evacuation of city children to the country, and so many speculative opinions put forward, that a careful study of the problems involved is especially welcome. This book describes a systematic survey, carried out both statistically and by case-study methods, of 725 Tottenham and Islington children billeted in Cambridge during the first six months of the war. The respective points of view of children, foster-parents, teachers, and local authorities (including billeting officers) were studied by means of questionaries, interviews, and essays written by the children. Unfortunately the survey had to be limited considerably both in scope and in method. The number of cases investigated formed only a small and not altogether representative sample of the evacuated population: the Tottenham children included few from very poor homes, and an unusually high proportion of adolescents; the question of the "under fives" could not be studied, since only twelve of the children fell into this age group. Also, the investigators were debarred from visiting foster-homes, and so were forced to rely on information gathered by willing but in most cases untrained "friendly visitors" of the W.V.S.

As the editors of this book recognize, the whole problem of evacuation is kaleidoscopic. Children and workers are constantly changing in any one area; conditions change with the varying phases of the war. Before the raids many foster-parents felt aggrieved at having to look after children whose homes were not apparently in danger. When the serious raids began there was a revulsion of feeling in favour of the temporary exiles, who in turn became more anxious on behalf of their families, with resultant nervous symptoms and disorders of behaviour; the lull in raiding has again made foster-parents—and parents—less tolerant. The Cambridge Evacuation Survey, though carried out before these changing circumstances became apparent, has gathered valuable information and formulated practical recommendations still of great use at the present time. Among the latter are the provision of more adequate hostel accommodation, including emergency hostels, the establishment of social and child guidance services, and the appointment of billeting officers chosen for their knowledge of the needs of children as well as of local conditions. The need for skilled planning and preparation, both in evacuation and in reception areas, is stressed, and various other suggestions are made for preventing the drift back to the cities.

The members of the survey are to be congratulated on having combined human insight with a scientific approach to material, and on a method of investigation that may well serve as a model for a larger and later survey of the problem.

A SURVEY OF CARDIOLOGY

Management of the Cardiac Patient. By William G. Leaman, jun., M.D., F.A.C.P. (Pp. 706; 255 original illustrations (2 in colour). 35s. net.) Philadelphia, London, Montreal: J. B. Lippincott Company. 1941.

This work, which purports to deal only with the treatment of heart disease, is in fact a comprehensive survey of cardiology. The presentation of cardiovascular disease comprises the orthodox descriptions of clinical methods, pathology, and physical signs, but the special claim to attention lies in the large number of case reports which illustrate the methods of treatment; pathological photographs of unusual excellence and well-considered records and diagrams are included. The desire of the author has clearly been to provide a practical treatise; this is manifest, for example, in the full details of therapeutics and in the well-thought-out schematic representation of diagnostic procedures.

Dr. Leaman's work is so far from limiting itself to treatment that it is hard to find any aspect of cardiology which does not receive consideration. Diet, air travel, social service, surgical procedures, physiotherapy, anaesthetics are reviewed in relation to heart disease; these sections are for the most part good, but some more conservative cardiologists might consider that the chapter on allergy and the heart should be omitted. No treatise on therapy in heart disease would be complete without a review of the surgery of the heart; the well-known procedures such as pericardial paracentesis, the operations designed to revascularize the heart muscle, and paravertebral alcohol injections are naturally included. How closely modern American conceptions of heart disease correspond to those of English cardiologists is observable at many points in this book; in one section—namely, registration of blood pressure—this standardization has been attained through the joint deliberations of the Cardiac Society of Great Britain and Ireland and the American Heart Association. Without any such collaboration nomenclature fortunately runs roughly parallel on both sides of the Atlantic. These facts, coupled with an easy style and the transparent zest of the author for his subject, combine to make this remarkable work not only instructive but arresting and readable.

The clinician picking up this new treatise on heart disease may see it at first as "another" cardiological textbook, but he will soon find that it is unusual in its conception, and exceptional in thoroughness and skill of execution.

MEMOIRS OF AN ANTHROPOLOGIST

A Jerseyman at Oxford. By Robert R. Marett. (Pp. 346. 15s. net.) London, New York, Toronto: Oxford University Press. 1941.

After the religious storms of the nineteenth century had subsided at Oxford and before the clouds gathered, so soon to break in storms of quite another kind, there was an interval of calm. Then it was that the youthful Marett came from Jersey as an exhibitioner to Balliol in the palmy days of Jowett's mastership. He had been strongly influenced by his ancestral environment. The granite island had accorded well with the temperament of its Norse invaders, who, however, gradually mellowed from contact with two civilizations. There Marett acquired an eager interest in the flora, fauna, and antiquities of the island, an admirable preparation for his life work.

Looking back on that golden age he found at Oxford, which must appear frankly incredible to the younger generation, he sees the happenings then as bright now "as the sun-lit air in which they first took place." And he skilfully conveys to the reader that happy atmosphere of academic life with its ardent friendships, noctes ambrosianae, and reading parties, yet with never a plaintive "eheu fugaces." His early devotion to biology and his philosophical studies converged, almost inevitably leading him to anthropology. Metaphysics he too often found "a glorified logic, as having sharpened a knife merely to brandish it in the air"; for him F. H. Bradley's *Appearance and Reality* "convulsed the mountain with his obstetrical attentions before extricating his mouse." The idea of an Absolute that knows everything and does nothing left him cold. So he became "an enthusiastic, if extremely ignorant, disciple of the school of Tylor," whose *Primitive Culture* had startled the world to the existence of a new

science, while the new light from Frazer's *Golden Bough* "dazzled his half-awakened eyes." Yet in his own earliest contribution—*Pre-animistic Religion*, in which he contended that ritual preceded belief—he departed from both those masters. He awoke to find himself "notorious," but to-day that view is widely held and his status as an anthropologist has steadily grown with the expansion of the subject.

In a sense, however, he declares anthropology was a hobby, for from the time that he became a Fellow of Exeter, a college of many associations with Jersey, his main work has been teaching and administration. At 75 he is still rector of that college, a post in which he succeeded the "iron vice-chancellor," Dr. Farnell. It is interesting to contrast this record of his happy experience in that office with the dismal memoirs of Mark Pattison, a somewhat earlier rector of the neighbouring foundation of Lincoln; so true it is that what one finds in a university largely depends on what one brings to it.

Dr. Marett has had a full life, blessed with good health and troops of friends. He tells us that he has never been troubled by an inferiority complex, and so much is evident in these pages. His optimism is, however, not based on mere levity. He tells us the last war "brought to a sudden end the long summer of my life": in the present one he lost a beloved son at Narvik; his ancestral home—La Haule—is in enemy hands, and of his sisters he can hear no word. Yet he can still reach the conclusion, "One can even be debonair about fighting the good fight, for, grim though it be, it is high adventure."

A delightful book, and though perhaps the fine bouquet of its vintage will be fully appreciated only by the seniors, all can be heartened in these dark hours by this self-styled "laughing philosopher."

Notes on Books

Many changes occur in the tenth edition of the popular pioneer member of Messrs. Churchill's series, and Dr. G. E. BEAUMONT and Prof. E. C. DODDS have carried out a thorough revision of their *Recent Advances in Medicine*. New material appears on such subjects as gastroscopy, electro-encephalography, the treatment of Addison's disease, and sternal puncture. Many will miss the section on basal metabolism, now omitted, and it is regrettable that the first chapter should be headed "The Sulphanilamide Drugs" when it is the sulphonamide group as a whole which is being discussed, with sections on sulphanilamide, sulphapyridine, and sulphathiazole. Nine pages seems little enough to devote to these important therapeutic agents. However, taken as a whole this volume maintains its high reputation and presents a well-digested survey of the medical advances of recent times. It is published at 18s.

Three authors—Dr. ARTHUR D. BELILIOS, Mr. DESMOND K. MULVANY, and Miss KATHARINE F. ARMSTRONG (Editor of the *Nursing Times*)—have collaborated in a *Handbook of First Aid and Bandaging*, published by Baillière, Tindall and Cox at 3s. 6d. The subtitle describes it as an "elementary and advanced course of training," and Surgeon Rear-Admiral Sir Cecil P. G. Wakeley says in his foreword that it is the most practical book of its kind that he has so far seen. It is compact, clearly written, and freely illustrated, and appears to us to be very good value for the money.

Physical Therapy for Nurses, by Prof. RICHARD KOVACS of New York, has now appeared in a second edition, published by Henry Kimpton, at 15s. Its subject-matter (from which *x* rays and radium are excluded) has been for many years the basis of postgraduate teaching to nurses and technicians at the New York Polyclinic Medical School and Hospital. For the new edition the text has undergone full revision, and there are new chapters on fever therapy, short-wave diathermy, and colonic irrigation.

Preparations and Appliances

A USEFUL ADDITION TO THE EQUIPMENT OF A MOBILE UNIT

Dr. A. BUCHANAN BARBOUR, chief medical officer to an air transport auxiliary, writes:

In the past a large number of people to whom it is often necessary to administer morphine have been trapped in "blitzed" buildings in positions not easily accessible. The following is the description of an appliance which I made some time ago, and which appears to be of service in these circumstances. I believe that mobile units and aerodrome crash crews would find it a useful addition to their equipment. It can be easily stowed in the unit's van.

The appliance consists of a light bamboo pole 5 to 6 feet long (Fig. 1), an end segment of which has been longitudinally divided,

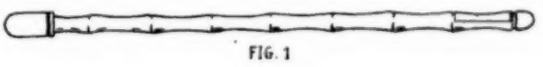


FIG. 1

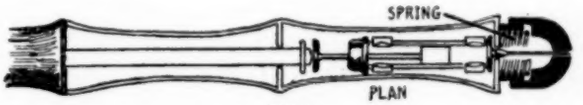


FIG. 2

FIG. 4 FIG. 3

FIG. 5

one half providing a small shallow compartment, the other detached portion forming a lid (Fig. 2). Into this compartment are fastened two standard Record syringe clips to take a 2 c.cm. syringe. In the centre of the end wall of this compartment a hole one-quarter of an inch in diameter is made to admit the shoulder of the hypodermic needle. Surrounding the protruding needle is a light spiral spring encased in a metal sleeve. The end face of this spring is attached to a metal dome, through the end of which in turn the hypodermic needle passes, a small channel being made to accommodate it. This dome-cover slides over the sleeve mentioned above (in practice a metal hotel-pattern salt-shaker has been found ideal). Down the remaining length of the bamboo pole a strip of round wooden dowling is passed, protruding about half an inch at the far end; its other extremity is in contact with the plunger-handle of the loaded syringe. A collar on the inner end of the dowling (Fig. 4) prevents its accidental withdrawal, while the external end is protected either with a metal cover or, what has been found adequate in practice, a 1-inch extension of the bamboo pole beyond the last knuckle (Fig. 5).

The syringe, having been charged with the desired amount of injection material, is loaded into the breech and fastened by the clips provided (Fig. 3). The needle is protected by the spring-loaded dome. The cover of the breech is replaced (this is easily fastened by a wide rubber band) and the pole is now ready for use. By pressing the end of the pole against an entrapped victim the dome shield recedes, allowing the needle to puncture the skin of whatever part of the victim is available (this may even be done through the clothing), the total extension of the needle being about half an inch. It then only remains to press the external end of the dowling for the contents of the syringe to be injected into the patient.

BRITISH MEDICAL JOURNAL

LONDON

SATURDAY OCTOBER 11 1941

SULPHANILYLGUANIDINE AS INTESTINAL ANTISEPTIC

In the past various drugs have been used as intestinal antiseptics, mainly without any sufficient evidence that they achieve the effect desired. Not only has any such drug to run the gauntlet of the several digestive secretions and to survive admixture with foodstuffs in successive stages of breakdown, but if it is to act in the lower bowel—and it is here that action is usually desired—it must escape absorption before the intestinal contents reach this area. This is asking much, and, in fact, none of the older intestinal antiseptics possessed all the qualities necessary to overcome these obstacles: those of coal-tar origin were certainly absorbed, because a tolerable daily dose mixed with the daily output of faeces would be actively bactericidal, whereas a corresponding effect was not demonstrable in the stools of patients under treatment. Now that sulphonamide compounds are becoming recognized as having a direct antiseptic action, and are being used more and more in the form of local applications, it is natural that inquiry should be made into the possibility of influencing the intestinal flora by their means. Sulphanilamide itself is much too rapidly absorbed to reach the lower bowel at all, and other less soluble compounds are not believed to reach it in any considerable amount. From a seemingly endless series of these compounds there emerges from time to time one which meets a therapeutic need previously unsatisfied, and although there was no reason for supposing that the peculiar qualities demanded of an intestinal antiseptic could necessarily exist in a compound of this class, such a substance has apparently been found. Sulphanilylguanidine, to which we made a brief editorial reference not long ago, has an action on bacteria comparable to that of its predecessors, but differs from them in being much less readily absorbed, with the result that much of the drug given by the mouth remains in the alimentary tract. This property is the more peculiar because the drug is fairly soluble; failure of absorption, therefore, does not mean that it remains in the bowel largely in a solid and therefore inactive form.

The brief history of this drug is given by D. E. W. Anderson and R. Cruickshank in their paper on page 497 of the present issue. The contribution of these authors to its study is a carefully observed therapeutic trial in bacillary dysentery, for which an extensive outbreak in a mental hospital provided the opportunity. This is a disease in which therapeutic effect cannot easily be assessed in quantitative terms, and the results claimed may seem unimpressive for that reason. It seems nevertheless that a decided amelioration of symptoms, more particularly in severe cases, was usually brought about within the first two days; that treated patients felt better and regained their appetite at an earlier stage; and that convalescence was shortened. More positive evidence of a specific action was that dysentery bacilli ceased to be recoverable from the stools at an earlier stage in treated than in control cases. Observations on this point were complicated by a change-over from MacConkey's to a more selective medium during the progress of the study; a culture medium which facilitates the detection of small numbers of dysentery bacilli is a valuable asset in such work, and the peculiarly selective action on Flexner dysentery bacilli of the medium described by W. J. Wilson and E. M. McV. Blair on page 501 may be found valuable in further studies of this kind. Anderson and Cruickshank's observations included estimations of sulphanilylguanidine in the blood, urine, and faeces. Blood levels, as claimed in the original American reports, were low, and heavier dosage would therefore probably be safe: it may be added that no toxic effects of any kind were observed in this series except a rash in one patient. Such of the drug as is absorbed is excreted in the urine, where fairly high concentrations are attained, and an adequate fluid intake appears advisable to prevent crystalline deposition in the urinary tract. Varying but mainly high concentrations were found in the faeces, and it was calculated that from one-half to two-thirds of the drug given remained in the bowel.

These authors do not record any general diminution in the numbers of bacteria cultivable from the faeces during treatment with sulphanilylguanidine, but quantitative methods of culture were not employed. Marshall claims that administration to mice causes a striking diminution in the numbers of coliform bacilli in their faeces, and according to W. C. Corwin[1] the effect in dogs and monkeys is not so much a reduction in total numbers of viable bacteria as an increase of Gram-positive cocci at the expense of Gram-negative bacilli. W. M. Firor and A. F. Jonas[2] found some diminution in faecal coliform bacilli in patients taking the drug, but the effect seems to have been neither consistent nor usually striking. These authors gave the drug for seven days before operations involving resection and anastomosis of the bowel, and obtained satisfactory union without peritonitis after complex and anxious proceedings involving gross contamination of the peritoneum. If this fortunate outcome is rightly to be attributed to the drug, then several kinds of intestinal bacteria other than the mere coliform bacilli and cocci which grow in ordinary aerobic culture must be severely curbed by its influence. It is clearly desirable to know more about the capacity of sulphanilylguanidine for restraining the growth of different types of intestinal bacteria before random clinical trial in the vast range of intestinal diseases gathers its inevitable momentum. The evidence of such an effect so far is scanty, and the bowel contents furnish so complex and apparently unfavourable a medium for chemotherapeutic action of this kind that success may well be partial and inconstant, or dependent on other factors which have yet to become known.

[1] *Johns Hopk. Hosp. Bull.*, 1941, **69**, 39.
[2] *Ann. Surg.*, 1941, **114**, 19.

THE AQUEOUS AND GLAUCOMA

Only fifteen years ago standard textbooks in ophthalmology spoke of the aqueous as a filtrate or as a secretion formed by the ciliary epithelium and eliminated via Schlemm's canal. The cornea was thought to be impermeable and was expressly excluded as a drainage path. The intraocular pressure was considered to depend upon the secretory activity of the epithelial cells of the ciliary processes. The fact that the intraocular pressure is supported by the corneo-scleral envelope was ignored, and the impossible assumption was made that the sclera was a rigid inextensible structure. Glaucoma was believed to result from the back pressure occasioned by blocking of Schlemm's canal, or from the mechanical consequences of increase in size of the lens with age, or from swelling of the vitreous. To-day no one would support all these statements and assumptions, and it may be of interest to summarize the views that are the outcome of modern research, although it cannot be claimed that finality has been reached.

The aqueous is a dialysate of the blood plasma, modified to a slight and as yet undefined extent by the activity of the epithelium of the ciliary body and perhaps of the iris; in addition there are the products of metabolism of the lens, vitreous, and lining membranes. Throughout the eye interchange of substances takes place in both directions across the capillary walls, particularly in the ciliary body and iris. In articles on the nature of the aqueous Friedenwald,[1] and Duke-Elder, Quillian, and Davson[2] deplore the fact that recent writers have again started calling it a secretion. In using this term most ophthalmologists have taken it to imply that intraocular pressure is the result of secretory activity, although this meaning need not be attached to the simple statement that the aqueous is a secretion. Friedenwald denies that the composition of the aqueous shows that water is transferred across the ciliary membrane to produce an accumulation of fluid on the aqueous side. The secreted fluid so transferred can be taken only from the lymph of the ciliary body and processes, and this lymph is certainly at intraocular pressure. The transposition of fluid across the ciliary membrane could not cause a change in pressure, as there is no change in the total volume of the fluid. It is precisely this total volume of the contents of the globe which determines the distension of the corneo-scleral envelope, of which the intraocular pressure is an expression. It is thought that fluid is drained out of the eye in the region of the angle of the anterior chamber, that fluid may then pass into the cornea or into Schlemm's canal, and that obstruction of the angle is associated with some forms of glaucoma. The cornea is certainly permeable, and evidence that it is a normal drainage path is growing. The significance of Schlemm's canal as a drainage path is not thought to be great.

The intraocular pressure is derived from the capillary blood pressure, with which it is in constant equilibrium. It is less than this pressure by an amount which is attributable to the difference between the osmotic pressure of the aqueous and the blood plasma; it may be quite small or be as much as 20 mm. Hg. The pressure within the eye, as in any other container, is a function of the distensibility of the walls—in this case of the cornea and sclera, which behave very much as an artery does when distended. At normal pressures the corneo-scleral envelope exhibits perfect elasticity, expanding and contracting with every pulse wave and responding to lid closure and other external pressure, as would a rubber ball. When exposed to abnormally high pressure, however, the envelope stretches and subsequently is much less distensible, so that it acts as a contributory factor predisposing to a recurrence of such raised pressure. This fact, and the increase in the rigidity of the sclera with age, are important to any consideration of the problem of glaucoma. Changes in volume of the lens and vitreous have no bearing on the problems: the former theory has no supporters to-day, and it has been shown conclusively that the vitreous cannot swell under conditions compatible with life. Workers are now almost unanimous in regarding the blood pressure, particularly the capillary blood pressure, as the source of the intraocular pressure in health and disease. The internal pressure in all the blood vessels within the eye is necessarily in equilibrium with the support accorded by the vessel walls plus the intraocular pressure. This equilibrium is modified to only a slight extent by changes in systolic pressure, since in the eye (as throughout the body) the expanding force of the blood pressure is precisely balanced by the ever-varying tone of the muscular elements in the vessel walls. Glaucoma is thus attributed to the transmission of an abnormal proportion of the available blood pressure within the intraocular vessels to the extravascular contents of the globe. Since the volume of the extravascular fluid contents—the aqueous—is rapidly adjusted by passage either into or out of the capillaries, the intraocular pressure must be related to the capillary pressure over any prolonged period. This equilibrium will not be modified by drainage of aqueous out of the eye via the angle of the anterior chamber. The intraocular pressure may be further modified, however, by a change in the osmotic pressure difference between aqueous and blood plasma; but this change is probably small and cannot exceed 20 mm. Hg. Research is thus directed to a study of those factors, nervous and chemical, which may modify the tone of the capillaries and arterioles in the eye and their permeability. Much progress has been made, and much is now known about these agencies. There is evidence that vasodilator or vasotoxic substances liberated by nerve action, formed locally as metabolites or entering the eye by the blood stream or via the cornea, may be the cause of clinical glaucoma.

[1] *Arch. Ophthal.*, Chicago, 1940, **24**, 107.
[2] *Brit. J. Ophthal.*, 1940, **24**, 421.

THE NUTRITION SOCIETY

Elsewhere in this issue we publish particulars of the newly formed Nutrition Society. In giving it, as we do, a whole-hearted welcome, we are not to be taken as either assenting to or dissenting from any general proposition about the desirability of forming new scientific societies—even in peacetime. For such projects to be praiseworthy at least two conditions must be satisfied. First, the subject of the new society's activity must be of importance—as the patent lawyers might say, it must have "content"; secondly, there must be no other existing society that can cover the whole of the same ground equally well. On the second issue the new society can claim general support. The scientific attack on nutrition is, indeed, made from many directions—by medical practitioners, biochemists and physiologists, agriculturists and veterinarians, dietitians and sociologists, economists, statisticians, food technologists, and probably others. In the specialized organizations to which these various experts belong questions of nutrition will be discussed with less or greater frequency. Indeed, in medical organization the attention given to dietary factors is certainly still on the increase. But even here, and in the excellent meetings arranged through its Nutrition Panel by the Food Group of the Society of Chemical Industry, it is obvious that there is a lack of integration. At the medical gathering the biochemist and laboratory worker are likely to be in the background, the agronomist and the practical dietitian probably entirely absent; at the Food Group meetings medical views are unlikely to be represented, and veterinarians are probably as invisible as statisticians. If the new society can bring together all the contributors to our growing knowledge of the relationship between food and health it will certainly achieve something not yet achieved—primarily, perhaps, because it has never been attempted, at all events in this country. And it has so far not been attempted because the importance of the subject is still too little appreciated in many of the most influential circles. It is doubtful if the emphasis given to-day to problems of feeding the community would have been nearly as marked but for the exigencies of wartime. In this sense, but we are sure in no other, the Nutrition Society may possibly be considered a child of Hitler. There can be little doubt to-day—least of all in the minds of medical practitioners—that nutrition has become a subject with "content." For the investigations of nutritional problems, special and other new techniques have been increasingly needed; for the discussion of problems and techniques alike a new organization has been found necessary.

That there are many gaps—some of them enormous—in our knowledge of human and animal nutrition would not be denied by the most craft-conscious nutritional scientist. The meetings or conferences to be organized by the new society—if one may judge by the proposed Cambridge meeting on "The Evaluation of Nutritional Status"—are just of the type calculated to reveal these gaps and therefore to point to ways of closing them. In that sense, if in no other, the foundation of the Nutrition Society may legitimately be regarded as a contribution to the national war effort, for it cannot fail to give support to all those forces that, by stimulating investigation and helping to disseminate its results, make for improvements in the dietary of the people as a whole and therefore in their health, their vigour, and their democratic independence.

MALARIA IN OFFICERS AND MEN FROM OVER-SEAS

It is important to remember that malaria is likely to occur among officers and soldiers who have returned to this country from service over-seas in a malarious country. The attacks may be relapses of a previous recognized infection, or they may be primary, especially in those in whom infection has been kept in abeyance by prophylactic treatment while in the endemic area. In the latter event a history of a previous attack may not be obtained, and the onset may be delayed for months after the cessation of prophylaxis. The need for early recognition and adequate treatment of cases of malaria is very great, and the possibility of this infection should be borne in mind in the presence of pyrexia without obvious cause, especially if associated with shivering, vomiting, and subsequent sweating, where there is a history of recent service in a malarious area. A high proportion of cases may be of the malignant tertian variety, in which severe symptoms may suddenly appear at the onset or later in the attack. If a patient shows clinical symptoms of malaria the lack of facilities for microscopical demonstration of the parasites in the blood should never cause delay in treatment, but before beginning anti-malarial remedies blood slides should be made for later confirmation of the diagnosis by microscopy. The War Office has issued a pamphlet, "Notes on the Treatment of Malaria occurring in Individuals returning from Service in Malarious Areas" (H.M. Stationery Office, 1d.), which will be of value to civilian medical practitioners as well as to Army medical officers. The lines of treatment concisely set out are grounded on Army experience, and they have been framed for the guidance of all who may be concerned. While the standard treatment detailed is that found to be best in the alleviation of symptoms and in prevention of relapse, and is the course recommended wherever possible, alternative lines of therapy are offered to meet circumstances in which certain drugs are not available. Precise instructions are given for the employment of anti-malarial drugs, Group A (quinine salts, and mepacrine hydrochloride) being anti-symptomatic and antipyretic and for treatment of the acute attack, Group B (pamaquin) being anti-infective and anti-relapse, for administration after the acute attack. Mepacrine is the British equivalent of atebrin and quinacrine; pamaquin is the British equivalent of plasmoquine; these two drugs must never be taken concurrently. There are brief directions for general treatment and for the handling of special symptoms. A section is devoted to intramuscular injection of quinine for heavy infections and severe symptoms. Another section prescribes the dosage and technique of intravenous injection of quinine for cases of great urgency, or for heavy infection with malignant tertian malaria, in which it may be the only means of saving life; it is fraught with danger and should never be used as a routine.

SCIENTISTS AND POST-WAR RELIEF

The British Association conference on "Science and the World Order," which was held in London during the last week of September, was a much larger affair than its promoters had looked for. The plan was to have a few papers to be discussed by British scientists among themselves, but men of science of other nationalities—some

of them exiles—proffered contributions, resulting in an amorphous conference, with sixty or seventy papers crowded into six sessions, with little or no time for general discussion or even effective presentation. The remarkable thing about the affair was its post-war spirit. So far as Albemarle Street was concerned during those three crowded days the war was already over, and all the hives were buzzing with reconstruction and relief after Armageddon. The problem was tackled from the point of view of the apparatus of government, of world planning, of technological advance, of biological teaching, and of social order and humanitarian aid. On this last subject Dr. Anni Noll struck a needed note when she begged the men of science not to forget, among much other reconstruction, the reconstruction of the family, already sadly disintegrated by evacuation and national service. One of the conditions of such reconstruction, she said, was the establishment of means of healthy living, from the point of view not only of medical attention but of housing, transport, food distribution, and facilities for education and leisure. She urged periodical overhauls of the family unit such as the Pioneer Health Centre at Peckham had sought to establish. A dark picture of nutritional deficiency in Europe, west as well as east, after the war was painted by a Continental medical man, Dr. Kodicek, who said that to prevent a major disaster plans for food distribution, the growing of food, and care of mothers, children, and sick would have to be organized with all speed. The help of separate Governments would be necessary, but they must work in collaboration under an international organization. Immediate help needed after the war would include medical supplies of all kinds, such as therapeutic sera and vitamin concentrates, also the training of doctors for service in distressed areas. An interesting statement was made to the conference by Mr. R. Allen of the American Red Cross, who has recently spent eighteen months in France, and has also been in Switzerland, Belgium, and part of Germany. In France since the German occupation the hospitals had been completely denuded of supplies and equipment, and the French had been left to set up hospitals in churches and schools, and to use surgical instruments purchased at hardware stores instead of through medical supply houses. The American Red Cross distributed hospital supplies alongside the German Army, from whom they had good co-operation. In non-occupied France children were being supplied with one pint of milk a day in the form of a specially reinforced powder, with added fat content and vitamins. He mentioned that the American Red Cross was now setting up in Geneva a reservoir of medicines and drugs for use in case of the development of any serious epidemics in Europe, of which there was a very real threat. It was trying to send medical and hospital supplies into Norway, Holland, Belgium, Yugoslavia, Greece, and occupied France. Among the less sombre notes struck in the conference was the plea of Mr. Philip Noel-Baker, M.P., for a sound food policy, with what Sir John Orr had called the minimum standard of maximum health as the starting-point in plans for post-war relief.

VITAMIN P AND CAPILLARY RESISTANCE

Manwaring and his co-workers[1] believed that "increased specific capillary permeability will be shown to be the dominant fundamental physiologic change in protein sensitization to which all other anaphylactic reactions are secondary." More recently Rapaport and Klein[2] have found forty-nine out of a hundred allergic children to have abnormal capillary fragility as determined by the Wright modification of the Rumpel-Leede test, using Wright's standard of ten or fewer petechiae as normal, from ten to twenty as borderline, and twenty or more as evidence of excessive fragility. In a previous study of 110 normal children only twenty-six, or 23.6%, had been found to show excessive capillary fragility as induced by a positive pressure test. Twelve of the forty-nine allergic children were found in subsequent capillary tests to be consistently abnormal. Vitamin P was administered and the tests gave normal results in all twelve. Ten of the twelve required only 100 mg. of vitamin P (as calcium eriodictate) daily, but the other two required 150 mg. daily, to bring about the "cure." Brown and Wasson[3] have measured the capillary resistance by the minimal amount of suction needed to produce one petechia or more when applied for one minute to the skin of the forearm just below the antecubital fossa. They found the average capillary resistance of 150 rheumatic children to be low, that it was subject to seasonal and climatic variations, and that the decrease in resistance which normally occurs with increasing age does not exist in rheumatic children. They also thought that severe reactions to injections of streptococcus filtrate might be related to low capillary resistance and to weather. They found a slight increase in capillary resistance in the treated over the untreated rheumatic children. They did not experiment with vitamin P therapy. Vacek,[4] using citrin prepared by two commercial firms, confirmed its influence on capillary permeability, its shortening of blood-clotting time, and its lack of influence on the thrombocyte count and bleeding time.

[1] *J. Amer. med. Ass.*, 1923, **80**, 303.
[2] *J. Pediat.*, 1941, **18**, 321.
[3] *J. Pediat.*, 1941, **18**, 328.
[4] *Schweiz. med. Wschr.*, 1941, **71**, 155.

RHEUMATIC FEVER AND STREPTOCOCCAL ANTIBODIES

After some sixty years of more or less intensive research there are now few infectious diseases of which the cause is entirely unknown. The great exception is rheumatic fever, where viruses, pleuropneumonia-like organisms, and bacteria have all from time to time been incriminated. In considering the aetiology of rheumatic fever, however, it is impossible to get far away from the haemolytic streptococci, although their exact relationship to acute rheumatism has never yet been accurately determined. The latest effort to arrive at some definite conclusion in regard to this relationship has been made by Mote and Duckett-Jones,[5] who have intensively studied the antibody responses to haemolytic streptococci in patients with acute rheumatic fever.

The characteristics of the sera investigated were their antistreptolytic and antifibrinolytic powers and the amount of precipitins against the C species-specific Group A substance of Lancefield,[6] the D, E, and K protein fractions of Heidelberger and Kendall,[7] and the P nucleoprotein fraction of Lancefield.[8] Before sera from rheumatic fever were studied investigations were made on sera from apparently normal persons. It was found that both the incidence and titre of streptococcal antibodies varied in the general population with age, general health, general economic environment, and the season of the year. Thus antibodies were highest in age groups 5 to 15 years, suggesting that numerous subclinical haemolytic streptococcal infections occur in this decade. As might have been expected, the occurrence of the several antibodies decreased as the economic level and the general standard of living

[5] *J. Immunol.*, 1941, **41**, 35, 61, 87.
[6] *J. exp. Med.*, 1928, **47**, 481.
[7] Ibid., 1931, **54**, 515.
[8] Ibid., 1925, **42**, 377.

increased, while the evidence showed that in the winter months there was a significant increase in streptococcal antibodies. It is thus not easy to arrive at any absolute value for the "normal" incidence of haemolytic streptococcal antibodies in a population. The normal level of antistreptolysin "O" in the control group, however, was concluded to be 150 combining units or less per c.cm. of serum, during the period of investigation. The antibody response was then studied in groups of patients with scarlet fever and with acute streptococcal pharyngitis; in both groups about 90% developed antibodies, frequently in high concentration, to one or more of the haemolytic streptococcal products tested. These antibodies could be detected in the blood for considerable periods of time. Analyses of similarly collected data from eighty-seven primary attacks of rheumatic fever revealed an equally high incidence of haemolytic streptococcal antibodies, whether or not there was a history of a preceding or an associated respiratory infection. Comparable data from 179 cases of recurrent rheumatic fever showed that in 73% antibodies to one or more of the streptococcal antigens appeared in the blood, often in high concentration, during the course of the illness. These antibodies persisted, sometimes for months after the onset of the infection, but finally returned to normal levels, even in the face of continuously active, sometimes even fatal, rheumatic infections. Mild or even severe recurrent rheumatic fever may, it seems, occur in rheumatic subjects without detectable clinical or serological evidence of a preceding or associated haemolytic streptococcal infection. On the other hand—and this is a subject which requires much further study—acute haemolytic infections may occur in known rheumatic subjects apart from recurrent rheumatic attacks. Both the rheumatic and the non-rheumatic subject, so far as antibody response is concerned, respond alike to infection with acute haemolytic streptococci.

The data brought forward by Mote and Duckett-Jones undoubtedly show that haemolytic streptococcal infection is often associated with acute rheumatic fever, but the essential mechanism responsible for producing rheumatic fever still remains unexplained.

BIOTIN, CO-ENZYME R, AND VITAMIN H

Biotin is an organic substance necessary for the growth of yeast. Co-enzyme R is necessary for the respiration of the root-nodule bacteria *Rhizobium* sp. Vitamin H is the substance which counteracts the ill effects of egg-white as a dietary constituent. It is almost certain that these three are one and the same substance. The unsuitability of dried egg-white as the sole source of protein in the diet of young rats has long been recognized and ascribed by various workers to the development of some toxic substance or to the destruction during the drying process of some hitherto unrecognized dietary essential.[1] In a series of papers during the last nine years H. T. Parsons and her colleagues[2-11] have shown that the toxic substance of dried egg-white, whatever it may be, is present also in the fresh substance; hence it is not generated during the drying process. They have also shown that the toxic effect can be neutralized by giving 20% of beef liver or various other foodstuffs. The curative substance in beef liver is partially destroyed by autoclaving at *p*H 8.0 for five hours, and it is entirely destroyed by ashing. Moreover, the ill effect of eating egg-white was not due to its antitryptic property. Kögl and his colleagues[12 13] have made crystalline preparations of biotin from egg-yolk, and have found that it is contained in watery extracts of various organs and tissues of dogs, cows, a male calf, and a laying hen. The liver, spleen, kidney, and adrenals were the best sources of the factor. Williams and his colleagues[14 15] have used the influence of biotin on the growth of yeast as the criterion for a quantitative determination of biotin. They used a thermocouple galvanometer for measuring the concentration of yeast cells in the medium at seeding and after growing with different additions of biotin. The medium found to be most suitable for the yeast contained sucrose, various salts, *l*-aspartic acid, inositol, β-alanine, thiamin (aneurin), and vitamin B_6. The method proved to be quantitative within a concentration range from 0.00002 to about 0.001 μg. (microgramme) of biotin. The following values of the biotin content (μg. per g.) of foods were determined: cane molasses 2.1 and 1.7, beet molasses 0.06 and 0.7, liquid whey 0.12, whey solids 2.5, fresh egg-white 0.05, fresh egg-yolk 0.37, autolysed egg-yolk 0.35, moist autolysed yeast 0.13, fresh potato 0.01, autolysed liver solids 3.89. Biotin is some fraction of "bios." Many of its chemical properties have been determined. It is destroyed by nitrous acid at a rate which indicates that it may be an α-amino acid. György and his colleagues[16] have found that both biotin and vitamin H are inactivated by benzoylation and acetylation and by the action of nitric acid. They have lately[17] identified a sample of crystalline biotin methyl ester prepared by themselves from a liver concentrate with one prepared by Kögl from egg-yolk, and by various methods of comparison have found them to have equal potencies with regard to vitamin H, biotin, and co-enzyme R activities. They therefore decided that the three factors are the same substance. Williams and his co-workers[18] have recently measured the biotin intake and excretion of chicks fed on egg-white injury diets and the biotin content of their tissues. They have concluded that biotin is useful to the chick and that egg-white is harmful in that it destroys the biotin normally present in the chick's food. Only when biotin is given in amounts more than sufficient to satisfy the egg-white will there be any available for the chick. More recently[19] the Cleveland workers (György *et al.*) and the Texas workers (Williams *et al.*) have collaboratively shown that the "toxic" substance in egg-white has albumin-like properties, and they have named it "avidalbumin." They concluded that it combines with the biotin, not destroying it, and that the compound so formed is excreted with the faeces. It has not yet been shown that biotin, vitamin H, or co-enzyme R is necessary for the human being.

On October 1 Sir Alexander Macgregor of Glasgow took office as President of the Society of Medical Officers of Health for the session 1941-2. He succeeds Dr. F. T. H. Wood of Bootle, who was elected for a second term of office last year.

[1] *Science*, 1933, **78**, 217.
[2] *J. biol. Chem.*, 1931, **90**, 351.
[3] Ibid., 1931, **92**, Proc. lxiv.
[4] *Amer. J. Physiol.*, 1933, **104**, 150.
[5] *J. biol. Chem.*, 1933, **100**, 645.
[6] Ibid., 1934, **105**, Proc. l.
[7] Ibid., 1934, **105**, Proc. lxvii.
[8] *J. Nutrit.*, 1934, **8**, 57.
[9] *Biochem. J.*, 1934, **28**, 2109.
[10] *J. Home Econ.*, 1934, **26**, 523.
[11] *J. biol. Chem.*, 1936, **116**, 685.
[12] *Hoppe Seylers Z.*, 1936, **242**, 43.
[13] Ibid., 1936, **243**, 189.
[14] *J. Amer. chem. Soc.*, 1940, **62**, 175.
[15] *J. biol. Chem.*, 1939, **128**, Proc. xxiii.
[16] *Science*, 1940, **91**, 243.
[17] Ibid., 1940, **92**, 609.
[18] Ibid., 1940, **92**, 224.
[19] Ibid., 1941, **93**, 477

THE ORGANIZATION OF AN EAR, NOSE, AND THROAT DEPARTMENT IN THE EMERGENCY MEDICAL SERVICE

BY

V. E. NEGUS, M.S., F.R.C.S.

Of all patients treated in the Emergency Medical Service a considerable proportion suffer from complaints affecting the ear, nose, and throat. A recent census taken at Horton Emergency Hospital showed that there were 114 patients in the wards set aside for the special department out of a total population of 1,500, the proportion thus being roughly one-thirteenth. Among the patients were 14 suffering from acute and chronic otitis media, 18 recovering from cortical and radical mastoid operations, and 2 on whom labyrinthotomy had been performed; 12 were in hospital for operations to correct deviation of the nasal septum, 21 were suffering from various forms of sinusitis, and 2 from carcinoma of the maxillary sinus; and 23 had been admitted for tonsillectomy. A variety of complaints were included in the remainder of the 114. This hospital has large orthopaedic and thoracic units; in hospitals with a smaller concentration of selected cases the proportion in the ear, nose, and throat wards would in all probability be higher.

The patients are divided into four categories, the relative numbers varying from time to time. There are civilian sick and civilian air-raid casualties, and Service sick and Service casualties. Among the Service cases are included Navy, Army, and Air Force personnel of both sexes, together with members of Allied Forces.

Segregation of Patients and Allocation of Special Wards

The specialized nature of the work and the inability to carry it out satisfactorily with patients scattered throughout the hospital, were in the early days of the war reasons for urging the necessity for segregation in wards set aside for the purpose. This request was met generously and with all possible collaboration by the medical superintendent of Horton Emergency Hospital, with the approval of the group officer. Similar assistance has been given by the superintendents of other hospitals in the sector, where special departments have been developed.

At Horton there are now two civilian wards, male and female, and two wards for Service cases, reserved for the head and neck unit; in them are housed all cases of disease affecting the ear, nose, and throat, together with patients suffering from injuries of these regions and of other parts of the head, including the eye. Two hundred beds are available out of a total accommodation of 2,000. The proportion of sick to wounded naturally varies from time to time. There are, however, at all times a large number of Service cases suffering from disease of the regions under question; they are admitted from a wide area.

Distribution of Special Clinics

In addition to Horton, there are in the sector other centres for ear, nose, and throat cases—at King's College and Dulwich Hospitals in London, at Sutton Emergency Hospital, the Blind School Hospital, Leatherhead, Cuckfield Emergency Hospital, and Horsham Base Hospital. Out-patients are seen at all these centres, and those requiring admission are taken into the appropriate hospital. Although the greater proportion of in-patients are treated at Horton, there is yet a considerable number at the other hospitals. It has been desired to develop efficient departments at each, with provision for medical and operative treatment, both for purposes of decentralization and to provide facilities for the immediate treatment of urgent cases of disease or injury. Certain types of case are transferred from the other hospitals to the main centre at Horton.

Medical Staff

A staff of part-time surgeons and whole-time assistants with special knowledge of the ear, nose, and throat has been allotted by the group officer, on whose co-operation the efficient treatment of cases depends. The senior surgeon is director of the unit at Horton and is in general charge of the work of the sector; he is also consultant to the department at Sutton and visits other subsidiary hospitals as occasion arises. There is a second surgeon in charge of two wards at Horton, acting also as consultant to the E.M.S. hospitals at Leatherhead and Horsham. A third surgeon, whose time is occupied mainly with administrative work, deals with certain cases at Horton and other hospitals, including Haywards Heath and Dulwich. Another consultant has charge of work at King's College Hospital and at Cuckfield. Whole-time registrars, each with considerable specialized experience, carry out much of the routine work under the direction of the consultants. Two are at Horton, one at Sutton, and one at Leatherhead. Of resident medical officers, two are attached exclusively to the department at Horton, while at the other hospitals work is carried out by residents, with additional duties. The variety and the amount of the material afford excellent opportunities for the higher education of resident medical officers and registrars.

Desirability of Special Treatment

It is thus seen that an organization is provided in the form of out-patient clinics and in-patient wards, with a staff adequate to deal with the large number of patients requiring attention. From the civilian economic view and also from the military aspect, this organization appears to be desirable. The effects of diseases and injuries of the regions under question are in the main temporarily disabling but amenable to treatment; the great majority of patients are returned to full efficiency if given appropriate care. The civilian is enabled to return to his work in full health and the soldier to his unit as a fit man, except in a very small proportion of cases. From the utilitarian point of view, both civilian and military, a patient with an infection or an injury involving, for example, a nasal air sinus is deserving of greater consideration than an air-raid or military casualty with fractured skull and laceration of the brain. The former should be cured, while the latter will in all probability be invalided out of his Service or civilian occupation.

Nursing

The nursing has been maintained at a high level of efficiency in spite of shortage of staff and other difficulties; and surgical results have been up to pre-war standards. The segregation of ear, nose, and throat and other head cases, under the charge of sisters accustomed to the work, has been of great benefit in every respect. The design of most of the wards at Horton is excellent for the purposes required. The subdivision of wards into sections and the provision of numerous small side-rooms allow separation of seriously ill from convalescent patients, while potentially infectious cases are readily isolated. Large galleries also are available to patients able to get out of bed, for meals and recreation.

Injuries and Diseases

The term "head injury" is often used to indicate cranio-cerebral conditions. If, however, a record is kept of all injuries to the head and neck admitted in unselected convoys it will be found that a large proportion concern parts of the head other than the cranium. Thus, of 577 head and neck cases out of a total of 3,917 casualties admitted to Horton between September 2, 1939, and May 1, 1941, 283 had injuries of the face, eye, nose, ear, neck, jaws, pharynx, larynx, and trachea. Injuries of the eye were most numerous, there being 126 cases, the face coming next with 87, and after that the ear with 74 cases. There were 14 wounds of the neck and 15 of the nose and sinuses, and 12 fractures of the mandible. The pharynx and larynx were each involved in one instance only, and the trachea in 3 cases. Wounds of all these regions present considerable difficulties and require the attention of specialists conversant with the surgical technique; the team must include not only ear, nose, and throat surgeons, but also ophthalmic and dental surgeons. Many patients have, in addition, injuries of other parts of the body, which must be looked after by general or orthopaedic surgeons; this applied to 82 out of the 577 cases under review.

Cranio-cerebral injuries are themselves often complicated by wounds of other regions of the head and neck, or of other parts of the body. It has been found desirable, therefore, to accom-

modate all cases of head and neck injury in the wards specially set aside, and subsequently to transfer elsewhere those requiring specialized treatment.

At the centres other than Horton the immediate care of the injuries referred to has been carried out by the special registrar, if available, or by other members of the staff, in consultation with the visiting ear, nose, and throat surgeon.

Instructions for the systematic treatment of ear and nose casualties have been circulated, with special reference to the prevention of inflammatory complications. Large mixed convoys invariably contain cases of injury or disease of these special regions, either alone or associated with other complaints. It is essential to have available an organization for their immediate and efficient care.

Of injuries to the ear, rupture of the tympanic membrane is the most common, and is of considerable importance. Precise notes were kept of 55 such cases at Horton; a considerable number occurred also at other hospitals in the sector. Antiseptic precautions, carried out early, combined with lack of interference with the deeper meatus, are the methods designed to prevent infection in the middle ear. Of the considerable number of such cases seen at Horton and other sector hospitals three have required subsequent cortical mastoid operation.

Attempts have been made to avoid secondary infection in surgical cases by the routine wearing of masks by all members of the staff when treating patients or carrying out dressings. Masks are worn during all attendances on such infectious cases as those with sore throats; nurses and others with colds wear masks whenever in contact with patients.

Diseases.—The emergency hospitals care not only for air-raid casualties and a proportion of the civilian sick, but also for large numbers of Service patients suffering from diseases of the ear, nose, and throat. A considerable number of Service out-patients have also been examined and treated at each of the five clinics. It is thus apparent that the organization set up for the treatment of casualties is turned to good use for the care of the sick of the Services, the great majority of whom are returned fit to their units.

Records of Work.—Tabulation of all cases admitted provides a ready means of reviewing the work done. Figures can rapidly be compiled to show the numbers admitted suffering from the various types of disease or from the results of injury. The indexing carried out by the registrars has proved of considerable value in compiling this and other reports.

Operations

At the beginning of the war the necessity for a specially equipped operating theatre, in charge of a sister with previous experience of this type of work, was impressed on the authorities concerned. Such a theatre was provided at Horton, and in it not only all the ear, nose, and throat work has been carried out, but also operations for various types of head injury. At the other sector hospitals the amount of specialized work has so far been insufficient to justify the setting aside of a separate theatre, even if such were available; the requirements of the work, differing from that of other branches of surgery, are, however, only to be fully satisfied in a specially designed theatre. The wisdom, at the beginning of the war, of admitting civilian cases of disease for operation in the emergency hospitals outside London was demonstrated by the development of an efficient organization during the months preceding the admission of casualties.

The large numbers of operations performed for disease have been of great benefit in perfecting arrangements for dealing with casualties. At Horton two operating tables can be used in times of stress, the theatre staff being sufficient to deal with many consecutive cases, both by day and by night. By co-operation with the hospital authorities various alterations have been carried out in fitting up the theatre, thereby raising it to the standard of efficiency required before the war.

The number of operations *for injury*, excluding cranio-cerebral and eye cases, performed between September 2, 1939, and May 1, 1941, is somewhat meagre. A certain number of patients had been operated on before admission, while many others, including those with traumatic rupture of the ear, luckily were saved from operation by careful treatment. A total of 66 patients required operation, including 15 on the ear, 13 on the nose and sinuses, and 5 on the neck.

Of *diseases* the variety is considerable, and is equal to pre-war standards. It says much for the efficiency of the theatre staff that operations such as labyrinthotomy, laryngectomy, and laryngofissure for malignant disease or stenosis have been carried out with satisfactory results. Of cortical mastoid operations, 12 were performed on civilian and 15 on Service cases, while 26 radical operations were required for civilian and 31 for Service patients. A total of 124 submucous resections of the nasal septum are included in the list, and 179 operations on the sinuses for inflammatory diseases and 15 for neoplasms. Tonsillectomy was necessary in 304 cases. Other operations brought the total performed on the ear, nose, and throat to 920 in the period September 2, 1939, to May 1, 1941.

Equipment

It has been made clear, in the preceding pages, that a large number of sick and injured patients require treatment in the hospitals of the sector and that ample accommodation and a trained staff are available for their care. Unfortunately the equipment which I consider necessary has not been provided. That supplied is insufficient in quantity for the many patients who must be examined, treated, and operated upon in this sector, and is in many instances of a different pattern from that to which my colleagues, my assistants, and I have been habituated. The return of civilians to their war work and of soldiers to their units should not be impeded by lack of equipment. We have had to improvise instruments and use privately owned ones to fill the gap. It is to be hoped that the importance of the ear, nose, and throat department in the Emergency Hospital Service will be recognized and that it will be equipped more satisfactorily in the near future.

TEMPORARY REGISTRATION OF OVERSEA DOCTORS

A new Defence Regulation and a new Order made under it by the Minister of Health and the Secretaries of State acting for Scotland and Northern Ireland extend the classes of doctors who may be registered by the General Medical Council for the period of the war. Under the Regulation formerly in force it was necessary for a doctor to be by law entitled to practise in a territory to which the Regulation was applied by Order, and this precluded a doctor from registration if he had passed the necessary examinations for a diploma but was debarred from practice by racial legislation or otherwise. The new Regulation applies to all territories without limitation, and puts persons who have passed the necessary examination in the same position as if they had obtained the diploma and become entitled to practise.

The combined effect of the new Defence Regulation and the Order is that a doctor who does not possess any United Kingdom qualification may now be registered temporarily if he satisfies the General Medical Council that he fulfils the following conditions: (1) that he is of good character; (2) that he holds a medical diploma (or has passed the examinations for a medical diploma) recognized as sufficient by the General Medical Council; and (3) that he has been selected for employment as a medical officer in an approved hospital, institution, or service, or as an assistant to a doctor on the permanent *Register*. Special provisions apply to persons selected for medical commissions in the British or Allied Armed Forces. The fact of registration does not affect the obligation of an alien to comply with the provisions of the Aliens Acts and Orders.

Further reference will be made to this new regulation in the *Supplement* next week.

W. N. Sarker and B. P. Tribedi (*Ind. med. Gaz.*, 1941, **76**, 257), who record five illustrative cases and emphasize the difficulties of diagnosis between uterine carcinoma and tuberculosis, have collected 3,744 unselected gynaecological biopsy specimens and 430 unselected necropsies in females between 1920 and 1940 for evidence of tuberculous lesions in the genital tract. The biopsy material showed an incidence of genital tuberculosis in 0.69%, while the necropsies showed an incidence of 8.9% in unselected deaths in females, and in 1.1% where death occurred from tuberculosis.

FOUNDATION OF A NUTRITION SOCIETY

Workers engaged on research on nutrition in this country have been feeling the need for a scientific society devoted specifically to their subject. In the past no organization has existed to enable investigators in the many and varied branches of the science—clinical, physiological, agricultural, and sociological—to find a common meeting ground for discussion and the exchange of views. Representative workers in all these fields accordingly decided to form a Nutrition Society. The new venture owed its inception to the following circular letter signed by the heads of some of the better-known centres for research on nutrition in this country.

Just before the outbreak of war a suggestion was made by several people interested in research on nutrition that a Nutrition Society should be formed. Owing to the outbreak of war the idea was abandoned. The question has, however, again been raised, and there are a considerable number of research workers and others in favour of holding meetings to discuss nutritional problems. Such meetings would serve a useful purpose, especially in enabling workers studying different aspects of the same problem in agricultural and medical institutions to meet and help each other with information and constructive criticism.

If there is a sufficient number of workers who wish to hold meetings for discussion of nutritional problems, the best procedure would be to form a society on the lines of the Physiological and the Biochemical Societies, although there would be no question of publishing a journal in the meantime.

In view of the difficulty of travelling it might be convenient to form separate English and Scottish branches, which would meet independently but which might maintain contact during the war by exchanging short notes on the papers and discussions at meetings.

Sir Joseph Barcroft, F.R.S. (Chairman, Food Investigation Board).

Dr. Harriette Chick (Head of Division of Nutrition, Lister Institute).

Prof. J. C. Drummond (Scientific Adviser to Ministry of Food, and Professor of Biochemistry, University College, London).

Dr. John Hammond, F.R.S. (Superintendent of Animal Research Station, Cambridge).

Dr. Leslie J. Harris (Director of Nutritional Laboratory, Cambridge).

Sir Frederick Gowland Hopkins, O.M., F.R.S. (Professor of Biochemistry, Cambridge).

Prof. H. D. Kay (Director of National Institute for Research in Dairying).

Sir Charles J. Martin, F.R.S. (Roebuck House, Cambridge).

Sir Edward Mellanby, F.R.S. (Secretary, Medical Research Council).

Sir J. B. Orr, F.R.S. (Director, Rowett Research Institute).

Prof. R. A. Peters, F.R.S. (Professor of Biochemistry, Oxford).

Subsequently a meeting was held at the Royal Institution attended by representatives from the various institutes, and the following provisional committee was formed: Sir John Orr, chairman; Dr. John Hammond, vice-chairman; Dr. Leslie Harris, honorary secretary; Mr. A. L. Bacharach, honorary treasurer; Dr. Harriette Chick; Dr. E. M. Cruickshank, Cambridge; Dr. H. H. Green, Veterinary Laboratory, Weybridge; Prof. H. P. Himsworth, University College Hospital; Prof. A. St. G. Huggett, St. Mary's Hospital; Dr. Franklin Kidd, Food Investigation Board; Dr. S. K. Kon, National Institute for Research in Dairying; Dr. B. S. Platt, Medical Research Council; Dr. H. M. Sinclair, Department of Biochemistry, Oxford.

It is, of course, not intended that the new society should compete in any way with existing scientific societies; its functions would be complementary to theirs, and would cover a more general and in some ways less specialized field. The main activity of the society at the start would be to hold meetings at various research institutes, at each of which some specific topic could be discussed: several main papers would first be read and would be followed by a general discussion. Arrangements have been made to hold the first conference of this kind at Cambridge on October 18, when the theme will be "The Evaluation of Nutritional Status." Contributions have been promised by Sir Frederick Hopkins (introductory address), Dr. Leslie Harris (Assessment of Level of Nutrition in Man), Dr. B. S. Platt (Clinical Signs of Dietary Deficiency), Dr. C. Crowther (Nutrition of Farm Animals). Among those who have promised to take part in the discussion are Dr. H. M. Sinclair, Dr. John Yudkin, Dr. G. W. Robertson, Dr. R. H. Dobbs, Dr. W. C. W. Nixon, Dr. H. H. Green, Dr. John Hammond.

Further particulars of the society can be obtained from the Honorary Secretary, Dunn Nutritional Laboratory, Field Laboratories, Milton Road, Cambridge.

Local News

ENGLAND AND WALES

Bristol Hospitals Commission

The Nuffield Provincial Hospitals Trust, having accepted an invitation from the Bristol and District Divisional Hospitals Council to make a survey of municipal and voluntary hospitals and ancillary services in Bristol and district, has appointed the following survey committee, to be known as the Bristol Hospitals Commission: Sir Farquhar Buzzard, Bt., Regius Professor of Medicine in the University of Oxford, and chairman, Medical Advisory Council of the Trust; Alderman Sir George Martin, vice-chairman, Provincial Hospitals Regionalization Council of the Trust; Prof. G. E. Gask, F.R.C.S., president, Medical Society of London, member of the Medical Research Council; Dr. M. T. Morgan, medical officer of health, Port of London Authority; Dr. John Buchan, medical officer of health, City of Bradford; Dr. J. P. Candler, late medical officer, Ministry of Health; Dr. A. Q. Wells, medical secretary, Medical Advisory Council of the Trust; Alderman W. Hyde, secretary, Nuffield Provincial Hospitals Trust; and Mr. S. Clayton Fryers, house governor and secretary, General Infirmary at Leeds. The terms of reference of the Commission are: "To take into consideration the present position of the voluntary and municipal hospitals and ancillary hospital and teaching services operating within the area of the Bristol and District Divisional Hospitals Council; inquire whether it is desirable that any steps be taken to promote further co-ordination or extension; consider how the existing and future services may best be financed and administered; and frame such recommendations as may be thought expedient and acceptable without prejudice to developments which subsequent inquiry may find to be desirable in other divisions in the projected West of England Region." The Commission has visited Bristol this week, with headquarters at the Council House. Preliminary work was undertaken by the Trust's officers. Each hospital has been invited to reply to a questionary, and the Lord Mayor has sent a letter to all contributory schemes in Bristol inviting them: (1) To submit observations on the present hospital accommodation and to make recommendations in regard to the future adequate maintenance and expansion of the hospitals and their progressive developments adequately to cater for the needs of the community. (2) To explain how, in their opinion, their organization can best help to solve the present financial problem of the Bristol voluntary hospitals, having regard to the principles on which the contributory scheme movement operates in the large cities, and how they can best help to implement the recommendations they have made under (1), assuming such recommendations to be acceptable to the hospitals.

Salaries in L.C.C. Medical Services

The London County Council recently revised the remuneration of certain of its district medical officers and assistant officers in consequence of a general diminution of work throughout the county, the reductions to be operative from September 1. Meanwhile representations were made to the Minister of Health by the officers concerned, and the Hospitals and Medical Services Committee of the Council received a deputation from the British Medical Association. As a result the Council, while satisfied that the proposed restrictions were justified in view of the amount of work actually performed during the period under review, is of opinion that some concession should be made, particularly in view of the fact that, irrespective of the reduction of work, there still remains the requirement that the district medical officer shall be available in his district, personally or by deputy, throughout each twenty-four hours. A revised scale of salaries has therefore been worked out, giving more advantageous terms to district medical officers with a small number of patients. This will have the effect of lessening the reductions in most cases by amounts varying from £5 to £25 a year. The earlier proposals would have resulted in a saving of approximately £5,020 a year; the new proposals will reduce this saving to about £3,740. The Council has also improved the salaries and conditions of service of certain medical staff at the Whitechapel venereal diseases clinic. New methods of treatment recently introduced make it unnecessary to provide medical attendance at all hours, and it is considered that, as nursing staff and orderlies are available at the clinic all day, the medical staff can more efficiently be employed for certain fixed times, which can be covered by each assistant medical officer working twenty hours a week instead of a minimum of thirty-six as at present. The assistant medical officers now receive yearly salaries varying from £375 to a maximum of £500, and are granted four weeks' annual leave and sick leave with pay. It is proposed that their remuneration henceforth shall be fixed at £500 a year, that their annual leave shall not exceed four weeks, and that they shall provide and pay approved substitutes during absence from duty through any cause, including annual leave.

Reports of Societies

THE ANALYSIS OF A PAIN

At a meeting of the London Association of the Medical Women's Federation, which was held at B.M.A. House on September 18, Dr. Janet Aitken presiding, Prof. J. A. Ryle gave an address on "the Analysis of a Pain."

It had always been an arresting reflection to him, said Prof. Ryle, that many of our most important and accurate assessments and decisions in medicine were based upon biological phenomena which we could neither see nor measure—that is to say, upon symptoms. In a recent essay he had drawn attention to the need for a much wider and deeper understanding of the two great primary symptoms which our patients bring to us—pain and fear. It was impossible to compute the number of lives which might be saved, the hours of suffering which might be curtailed, the illnesses which might be shortened, and the increase in working hours which might be obtained if only the fullest use were made of what we already know about the physiological import and consequent clinical interpretation of many types of pain. And what a lot there was still to be discovered! A symptom, he reminded his audience, expressed a physiological dysfunction, a sign, a structural alteration. A physiological dysfunction was in the direction of either an exaggeration or a depression of a normal process. We could often trace the gradations between a "symptom" of health—such as hunger—through the symptom of health modified by stress to the symptom of developed disease, as he would endeavour to illustrate. We often spoke of the "symptom of a disease"; this was incorrect, for symptoms, while specific for disturbances of function, were not specific for pathological changes.

Why did so many pains, even including some of the more classical and familiar varieties, go so often unexplained and unrelieved? Because we had not been taught to systematize our inquiries into subjective phenomena with one-tenth of the thoroughness with which we had been taught to systematize objective studies. The more the use of objective measures was extended and elaborated the more, it seemed, did we tend to neglect the analysis of subjective phenomena, which often permitted precise diagnoses even when "other investigations" were unavailing. What was needed to remedy existing deficiencies in method and knowledge? First, better clinical education; secondly, better habits of observation and record in practice; and, thirdly, planned experiment as advocated and practised by Sir Thomas Lewis and his school. It was in the power of all in practice to improve their observational method. In respect of any pain we required an anatomical, a physiological, a pathological, and a psychological diagnosis; to know, in other words, where it originated, how it was produced, by what agency it was stimulated, and to what extent it was modified by temperament, mood, and sensibility in the individual case. Biological purpose should also be philosophically pondered. He emphasized the importance, whenever possible, of seeing patients when actually in pain, and advocated a pain questionary, including twelve points relating to character, severity, situation, localization, paths of reference, duration, frequency, special times of occurrence, activating or aggravating factors, relieving factors, associated symptoms, and elicited pain or tenderness.

Anginal Pain and Hunger Pain

Prof. Ryle then proceeded to an analysis of anginal pain and hunger pain on the basis of such a questionary. In the case of angina pectoris he pointed out how mistakes in favour of a diagnosis of "dyspepsia" could sometimes be traced to the occurrence of the symptom after food; close inquiry always showed that it was exercise after food which caused the symptom. He asked his audience to consider whether Lewis's conclusions in regard to the physiology of anginal pain arrived at by clinical experiment might not have been forecast on the basis of more careful clinical observation. Anginal pain was encountered in coronary occlusion, coronary sclerosis, aortic disease (rheumatic and syphilitic), the overactions of the heart accompanying paroxysmal tachycardia and hyperthyroidism, severe anaemia, tobacco excess, and emotion. Coronary occlusion and anaemia should have given the clue. The only common factor in all these conditions was the unfavourable ratio of work to oxygen supply, or a relative anoxia of the cardiac muscle. Anginal pain was, in fact, found to be specific for a physiological disturbance and not for a "disease." It would seem to have a direct biological purpose, acting as a warning, and a very impressive one, that the patient's capacity for work was strictly limited and his heart in jeopardy.

A similar analysis of hunger pain showed it to be specific for a certain dysfunction which could be described as an exaggeration of the tonic and peristaltic muscular phenomena that characterize normal hunger and not for any single disease such as duodenal ulcer. It was relieved by the same factors which relieved hunger; it was often accompanied by water-brash, which could be regarded as an exaggeration of normal mouth-watering, and by the same general irritability as observed in natural hunger. Biologically it could be argued that those things which relieved it also relaxed the too tense muscle fibres and buffered the gastric acids and so helped healing when the provocative factor was an ulcer. Biological purpose in the case of pain should not, however, be too strongly pressed, and could not always be adduced, even though in injury and angina the pain might seem to have a clear and benign use.

In conclusion he did not insist that every busy practitioner must subject all his patients with pains to such an exhaustive symptom-analysis as he had outlined. Life was too short. He did suggest, however, that such analyses were valuable in difficult cases, that they added interest and achievement in a diagnostic sense to the experience of practice and made for clearer and deeper thinking about the everyday natural phenomena of disease. Other subjective phenomena besides pain could be studied by a somewhat similar approach. We could not and should not dispense with objective methods. We should always prefer measurements to qualitative assessments. But we should also remember that human sensibility and sensitivity were so delicate that they often led to accurate decisions long before eyes or hands or instruments could make their contribution or guided and modified opinion when other evidence was forthcoming.

Correspondence

R.M.B.F. Christmas Gifts

SIR,—Old customs and traditions are greatly valued and treasured by elderly people: memories of past days are very precious, perhaps none more so than those of happy Christmas Days gone by.

For many years your readers have most generously supported my appeal on behalf of the Christmas Gifts Fund of the Royal Medical Benevolent Fund and the annual distribution of a gift of 30s. has brought great happiness to our beneficiaries, many of whom are old and lonely. I have now been president of the fund for nearly twenty-five years, and would like to thank all who have responded to my appeal in past years and have every confidence that this year the same kindness will be shown. With an additional contribution we could raise our gift this year to £2 instead of 30s., which would give so much pleasure.

Will contributors please address to Christmas Gifts, Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15, and their gifts will all be gratefully acknowledged.—I am, etc.,

THOS. BARLOW,
President.

Oct. 1.

Voluntary Hospitals

SIR,—I have been interested in the answers to Sir Frederick Menzies's question. Most of the answers I have read give me the impression that hospitals are run for the benefit of the medical staff. Nobody will disagree with the view that the voluntary system is ideal for achieving freedom for the medical staff. To achieve this freedom is not, however, the prime reason for running hospitals; they are intended for the treatment of the sick, especially the sick poor. What we have to arrive at is the best system of dealing with the sick who need hospital treatment.

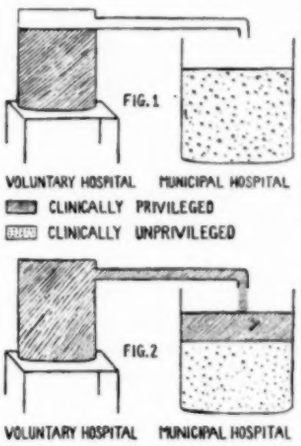
The question of the freedom of the staff, especially the clinical freedom, is obviously important, but only subsidiary, and should only be considered in its proper relationship to the primary objective. Let us think in terms of the patient. I wish to contend that the voluntary system is not a system but a very incomplete part of a chaotic arrangement which has arisen in the following way:

Though the voluntary hospitals set out to deal with the sick poor, it became obvious some forty years ago that they were dealing with only certain of the sick poor. They were dealing with those who were privileged to have acute illness and accidents which were amenable to surgical intervention, or those medical cases which were interesting and not too chronic. They were dealing with the clinical wine—but what about the clinical draught beer, much greater in volume, much less palatable and interesting? These patients, the clinically non-privileged, had to find shelter in the then Poor Law hospitals, where they were kept, in the words of the official reports, "clean and well cared for." So that by 1920 the situation was as in Fig. 1 (after the manner of the renal threshold diagram).

Round about this time the voluntary hospital chalice began to overflow. Clinical wine began to trickle over into the municipal pint pot. Immediately this clinical material began to arrive municipal hospitals woke up; as the material arrived so the staff and equipment were mustered. Tentatively at first, and with many blunders, the best method of staffing had to be evolved, and still has to be evolved. The situation at present can be represented by Fig. 2.

Yes, the voluntary system certainly has the virtue of freedom which the municipal hospital has not got. It is free to pick and choose its patients according to their clinical possibilities; but it would not be free to do so unless the municipal hospitals were in the background to deal with those conditions which the voluntary system did not choose to deal with. If you are a keen worker for your local voluntary hospital, pray that when you become ill you will be privileged to have the right sort of illness if you wish to get a bed in your hospital; if you do not have that good fortune do not worry too much. There will be a bed for you in the municipal hospital. There will be nurses to look after you, residents of some seniority to examine you, and consultants of high rank to help you over your trouble. These officers may not be perfectly free, but the best of them will have a well-developed professional conscience, and the worst of them are not likely to be less troubled by this corrective than under the voluntary system.

Up to the present time the municipal system has been occupied in filling in the gaps left by the voluntary system. The problems of the two systems are hardly similar enough yet to warrant any form of comparison, particularly as regards medical staffing.



Six years as a resident in voluntary teaching hospitals and fourteen years as a resident in municipal hospitals with teaching-school consultant staffs have shown me that good men will do good work whatever the system, and I am grateful for having had the privilege of sharing in this work under both systems. I believe that all hospitals should have a chronic annexe, and that no patient should be transferred there until every investigation has been made. This would eliminate the classification of clinically privileged from clinically unprivileged, and would give many other advantages too numerous to mention. I believe that all the resources of any given region should be unified to produce regional hospital schemes. I believe that hospital services should be planned. Planning must curtail freedom to some extent. Only planning can give the best service, and in a noble cause the "best service is perfect freedom."—I am, etc.,

E. S. CLAYTON, M.D., F.R.C.S.Ed.,
Medical Superintendent, Manor Hospital.

Walsall, Sept. 29.

SIR,—I think your readers will agree that the questions with regard to the voluntary hospital system which I posed in my letter of September 6 (p. 353) have evoked some interesting replies, and, incidentally, they have brought me a number of private letters as well. It would be impossible within the limits of space available to comment upon every one of the letters published in your issues of September 20 and 27 and the private letters referred to above, and I must therefore restrict myself to those matters which seem to be of outstanding importance.

Certain of the "best features of the voluntary hospitals system" put forward include (*a*) the importance and value of tradition and prestige; (*b*) the religious spirit which animates their activities, particularly the nursing staff; (*c*) the Christian virtues associated with the dependence of voluntary hospitals upon charity; (*d*) the personal service without immediate reward, as exemplified by the governing board, nursing and medical staff; (*e*) the independence of the voluntary hospital units, described as something essentially characteristic of English institutions, leading to such desirable virtues as self-reliance and self-dependence; and (*f*) the medical work done resulting in the staff being among the best men in the medical profession. These examples are not meant to represent a complete catalogue, but they suffice to illustrate the general trend of the correspondence. In addition, it is necessary to take note of the fact that there seems to be a general consensus of opinion among supporters of the voluntary hospital system that the medical superintendents of the municipal hospitals are the "evil men" of the municipal hospital service.

Far be it from me to decry the immense importance and profound influence for good which are inherent in such virtues as tradition, prestige, the religious spirit, charity, personal service, independence, self-reliance, etc., but I confess I find it very difficult to believe that these are features which can truthfully be described as characteristic of the voluntary hospitals of to-day. Tradition and prestige may still be true of some of our oldest voluntary hospitals with centuries of devotion to the sick poor behind them, but the vast majority of our voluntary hospitals are quite modern institutions, having neither tradition nor prestige, nor any pretensions to them, any more than the secon-

dary schools have to the tradition and prestige of the oldest of our public schools. Similarly, the religious spirit and charity so emotionally described in Dr. Geoffrey Evans's letter are hard to reconcile with the economic conditions which we all know to-day compel medical and nursing and all other hospital staff to think, and to think hard and realistically, in terms of salaries and wages, and to press their demands with no uncertain meaning upon their employers, whether national, municipal, or voluntary. Likewise it is surely inaccurate to say that the voluntary system depends to an extent upon charity, when "charity" in the proper sense of that word in actual practice means that every hospital chairman and secretary is racking his brains for some new method of raising money to supply the essential needs for the proper care of their patients. Bridge parties, matinées, students' clownish processions, nurses in uniform with collecting boxes at street corners, disfiguring advertisements on the walls of hospitals setting forth the virtues of some proprietary food or drink, and so forth, do not seem to me to breathe the real spirit of charity.

Personal service, whether it be exemplified by the governors or the nursing and medical staff, *without immediate reward*, is not a virtue peculiar to the governing boards of voluntary hospitals, and is certainly untrue of both the nursing and medical staff, inasmuch as the nursing staff are paid like any other staff and the medical staff have in their capacity as members of the hospital staff their biggest asset in creating a remunerative private practice. The term "honorary" staff is to-day a misleading description, but useful as one of the items included in appeals for subscriptions, donations, and legacies. Independence and self-reliance, properly practised, are admirable virtues, but who is there to-day who is prepared to deny that the independence of voluntary hospitals, as hitherto understood, has been carried to such an extreme that it has almost precipitated their downfall? Indeed, is it not true to say that this very independence has almost succeeded in destroying democracy? Nor do I agree with the wholesale condemnation of the medical superintendents of municipal hospitals. If I were challenged to do so I could without the least difficulty recite the names of many medical superintendents who during the last forty years have done magnificent work in their hospitals and whose example of high devotion to duty is among the treasured memories of many scores of those younger members of our profession whose good fortune and privilege it was to work with them. The simple truth is, of course, that just as there are voluntary hospitals and voluntary hospitals, so there are medical superintendents and medical superintendents; and therefore generalized "boosting" of the voluntary hospitals as if every one of them possessed even those features which we all agree are "their best features" is just as silly as general condemnation of all medical superintendents and the attribution to them of those bad features which we all wish to remove from the municipal hospitals. In this connexion here are very brief extracts from a memorandum recently written by a distinguished member of our profession which should give Dr. Geoffrey Evans and his friends pause to think realistically and not emotionally.

> "The weakness of the present system of staffing voluntary hospitals lies in the fact that the services rendered by the medical man to the hospital are not his primary concern. They are essentially secondary, a means to an end, the end being the development of an adequately remunerative private practice. . . . The voluntary hospital system at present suffers in so far as its service is subordinated, consciously or unconsciously, to the influence of private practice."

These words, and many more like them, severely condemning present conditions in our voluntary hospitals were recently written by an eminent voluntary hospital man and endorsed by a number of equally eminent members of the staffs of our voluntary hospitals throughout the country. What about tradition, the religious spirit, charity, personal service, etc., after all that? And here I would remind your readers that there are a large number of lay men and women in this country who devote themselves whole-heartedly, and often at great personal sacrifice, to the direction and management of the heavy duties and responsibilities of local government, including the public health and hospital services, and also that if Dr. Geoffrey Evans and his friends really wish to see the best example in this country of the "Florence Nightingale" nursing spirit they should go and spend a week or two in one of our large municipal hospitals for the care of the chronic sick.

Dr. Malcolm Donaldson is right when he says he hopes "to see very drastic reforms in the near future in the voluntary hospitals." So do I when I think of the grossly overcrowded out-patient departments, with patients waiting for hours to be seen and more often than not ultimately examined superficially by a junior and quite inexperienced member of the medical staff and sent away with a bottle of medicine or a lotion or bottle of lozenges, or again when I think of the pride with which one is told that there are some hundreds of patients on the waiting list for admission, many of whom will have no chance of a bed for weeks or even months, and so forth. It would be easy to extend the catalogue of the worst features of the voluntary hospitals, but that is not the question to which one wished for an answer, any more than one asked for abuse of the medical superintendent. It appears to me that the nearest approach so far to an intelligent reply to my questions is contained in the admirable letter of Mr. Lang Stevenson (September 27, p. 456). The third paragraph of his letter gives a brief but excellent exposition of the "best features of the voluntary hospital system," but I think it is probably true to say that they are only to be found in most of our teaching hospitals and in a very limited number of non-teaching hospitals. I do not suppose that Mr. Lang Stevenson means to suggest that his description is characteristic of the voluntary hospital system generally, but only of the best of the voluntary hospitals. Nevertheless, they are the features we want to preserve. I find myself wholly in agreement with the eight suggestions he makes for removing some of the defects of the municipal hospital system, and I am happy to think that practically all of them were actually introduced into the L.C.C. hospital service between 1930 and 1939, as well as quite a number of other county hospital services within my personal knowledge. It would scarcely be possible to point to a hospital, voluntary or municipal, in this country which more nearly approximates to the ideals of the best type of hospital than the British Postgraduate Hospital and Medical School at Hammersmith. Before war broke out that hospital was characterized by the unique combination of a medical staff devoted entirely to clinical work and research and an L.C.C. medical staff which took over the entire control of the administrative work of the hospital.

Finally, may I add that in this matter of the best features of the voluntary hospital system there is too great a tendency on the part of voluntary hospital supporters to think of voluntary hospitals in terms of the best of our teaching hospitals, and to assume that what is true of our teaching hospitals is equally true of all of our voluntary hospitals. Similarly there is still a tendency among voluntary hospital supporters to think of the municipal hospitals of to-day in terms of the old Poor Law infirmaries of pre-1930. This is a profound mistake. Much has happened in the matter of improvement in the municipal hospital service since the Local Government Act, 1929, came into operation on April 1, 1930, and much more still would have happened in the next ten years had it not been for the outbreak of war. For the moment progress is arrested, but in due course progress will be resumed. The municipal hospital service is only a few years old; it has gone through a very difficult period of transition in 1930-9; it was well beyond its "teething troubles" before 1939. The voluntary hospital system has been in operation for centuries and has been fortunate in every respect in the support which it has attracted from all classes of society and all ranks of the medical profession. Hence one's desire to obtain a clear picture of what is meant by its best features, how far it would be practicable to introduce them into the new municipal hospital service which we all know has come to stay and which may indeed in the near future become the only hospital service. From that point of view the correspondence published up to now in the *Journal* has been helpful, but not, I confess, quite so helpful as one had fondly hoped.—I am, etc.,

Criccieth, Sept. 30. FREDERICK MENZIES.

Medical Education

SIR,—Those who have not had experience of teaching physiology will agree with your recent leader (September 6, p. 340) that clinical cases would be of benefit in teaching, say, the nervous system, but those who have tried this have been grievously disappointed in its results. Many years ago Halliburton, in conjunction with Mott, tried this and found it a failure, but finding

this difficult to understand I, too, have tried it, with similar results.

The difficulty is that the non-clinical student has not yet become accustomed to the sick man and takes such a great interest in his clothes and in the human side of the cases generally that he fails to pay attention to the reactions of the nervous system. There is no doubt that applied physiology should be taught, but it should be when the students have become accustomed to clinical examinations and preferably have had six months' medicine and surgery. Then, as has been my experience at St. George's Hospital, students become almost embarrassingly eager to learn the exact scientific explanation of signs and symptoms.—I am, etc.,

London, Sept. 27. R. J. S. MCDOWALL, M.D.

SIR,—I was greatly interested in your academic issue of September 6 and in the correspondence evoked by its contents so far. We are living in an age of change and transition, and in this may safely be included medical education. The articles by the teacher and the taught on the subject are very fraught with possibilities, and your leading article contains much good meat. Representing neither teacher nor taught, but working in the non-academic medical realm, I feel some things need to be said.

In teaching medicine and surgery, and their ancillary subjects, I feel it would be far better if those members of the staff who had a flair for teaching did the work. Clearly, in a hospital, some physicians and surgeons are obviously pure clinicians, whereas others are that and teachers as well. Lectures and ward rounds and out-patient sessions should be left to those who know how to teach and, as we say colloquially, "know how to put it across." In commerce good salesmen study window-dressing, so in medicine academic window-dressing is urgently needed. A man may be a specialist, for example, on cardiac disorders and yet may be a very poor exponent of his knowledge on that subject. The art of lecturing needs as skilful preparation as does, for example, the art of surgery. Lectures have fallen into disrepute, and deservedly so, because some lecturers do not present their material in an attractive and palatable form and usually have a very small background of classical training. The same principle holds good for writers of textbooks.

The curriculum, as constituted, is for the most part satisfactory, but needs to be more practical in some places. The main subjects of medicine, surgery, and pathology are well taught, but some of the special subjects need better arrangement—for example, diseases of the eye, ear, nose, and throat. Queueing up to see an optic disk or a tympanic membrane is unsatisfactory. Gynaecology could be better dovetailed in with surgery, and obstetrics left to stand by itself. In view of its vital importance more time should be devoted to obstetrics, a subject combining medicine, pathology, and surgery. Another vital subject is anaesthetics, which is important in all medical spheres: one month's clerking and some six lectures are not good enough. Public health problems deserve more stress than at present in maintaining the national health and in prophylaxis against infectious diseases and other grave scourges.

Psychological medicine is coming more and more into its own and deserves better treatment. My teacher, E. B. Strauss, teaches that "psychiatry is the other half of medicine itself." Organic disease is so often founded on the bedrock of mental stigmata, and few doctors leave hospitals with an adequate psychiatric background and recognize patients as human beings rather than cases. More attention should be given to dietetics and to applied pharmacology, the basis of all true rational therapeutics.—I am, etc.,

Norwich, Sept. 24. J. B. GURNEY SMITH.

Carriers of Tuberculosis

SIR,—We were very interested in the article on carriers of tuberculosis by Dr. James Maxwell (May 3, p. 665). It is interesting to note that Pendrill Varrier-Jones, in a lecture delivered in 1919 to the Royal Institute of Public Health, entitled "The Future of the Tuberculosis Problem," stated:

"Is it a fact, for example, that just as there are carriers of the germ diphtheria so there are carriers of the tubercle bacillus, who go through life without any symptoms which might at any time attract attention, and yet are the means of handing on the disease to several, nay many, persons? I might illustrate the point by a concrete example. A Cambridge undergraduate, a fine athletic man, developed what was diagnosed as an attack of influenza. Its course was prolonged and there was cough and expectoration. The sputum was examined repeatedly with negative results. The patient recovered completely. Some months afterwards he suddenly coughed up a mass of sputum, and being of a curious turn of mind brought it to the pathological laboratory with a request that it should be examined. Under the microscope the specimen was almost a pure culture of tubercle bacilli, so numerous were the rod-shaped organisms. The patient was apparently in the best of health. It may be argued that such a case would be very difficult to discern, very difficult to isolate, and it may well be that, among the well-to-do, those who live under the best conditions, the disease is spread by such an individual as I have just discovered."

The late Sir Pendrill Varrier-Jones was always insistent on the fact that tuberculosis carriers were a source of great danger to the public health, and was, we think, the first individual to draw our attention to the presence of carriers of this disease.—We are, etc.,

Clinical Department,
King George V Hospital,
Durban, Aug. 19.

B. A. DORMER.
J. FRIEDLANDER.
F. J. WILES.

Tuberculosis in Glasgow

SIR,—The paper by Dr. Stuart Laidlaw and Dr. Duncan Macfarlane on the recent increase in the incidence of and mortality from tuberculosis in Glasgow (September 27, p. 436) raises points of special interest at the present time. They attach chief importance to overwork, strain, and curtailed rest as factors responsible for the increase in the notifications and deaths which they record.

The conditions which predispose the human body to active invasion by tubercle bacilli are varied, and it is not always possible to attribute to any particular factor its true position of relative importance. Drs. Laidlaw and Duncan are no doubt correct in concluding that strain is one of the principal aetiological factors, more especially if we accept the definition of strain as a prolonged over-call on physical, mental, and nervous energy. One of the effects of war on the civil population which was observed during the years 1914-18 was loss in weight irrespective of whether the individual was doing heavy manual work or not. Such loss in weight is due to one of two causes, or to both—namely, diminished intake of fats and proteins and increased metabolism arising from physical, mental, or nervous strain, and when it affects members of the young adult age group it is usually associated with impaired nutrition and diminished resistance.

The relationship between strain and nutrition should receive special attention at the present time. Apart from specific protection, resistance to tuberculosis is governed by the standard of nutrition and the degree of local resistance. We are liable to view the state of nutrition as depending exclusively on the amount and character of the food taken, but the standard of nutrition may be seriously impaired by strain and overcrowding. Emerson (*Nutrition and Growth of Children*, 1922) has drawn attention to the importance of over-fatigue as a cause of malnutrition in children and, consequently, as a factor in the incidence of tuberculosis. In the report on tuberculosis in Wales (*Anti-tuberculosis Services in Wales and Monmouthshire*. Report of Ministry of Health Committee, 1939) reference is made to the possible influence of stress or strain in increasing the injurious results of dietary deficiency, or in causing them to appear in persons who previously had shown no evidence of such deficiency. In a recent publication (*Tuberculosis and National Health*, 1939) I have stated that "war, especially when prolonged, leads to increase in the incidence of tuberculosis. Resistance is impaired by strain, fatigue, trauma, and interference with the normal supply of food, while the risk of infection is increased by overcrowding and the mass movements of population."

One point of significance to which Drs. Laidlaw and Macfarlane draw attention in their paper is the influence of curtailed rest and ill-spent leisure in promoting strain. One hesitates to suggest any curtailment of reasonable amusement and recreation for young people doing exacting manual work, but it is obvious that late hours under conditions of overcrowding and with inadequate ventilation due to lighting restrictions cannot but induce added strain and lead to impaired nutrition. Rest and sleep are essential for the young

adult to counteract the effect of physical, mental, and nervous strain.

The Government has wisely taken action to make a fairly balanced diet available and to provide additional fat-forming foods for certain groups of the population. The greater the amount of strain to which any section of the population is exposed the greater the need for an adequate intake of balanced articles of food. The Government has recently taken further steps in this direction by increasing the quantity and improving the variety of food for those undertaking heavy manual work. It would appear desirable, however, that some guidance should be given, especially to those in the young adult female age group who are doing work involving much strain, as to the need for rest and sleep, and as to the character of the recreation which is least likely to be injurious to health.—I am, etc.,

Helensburgh, Oct. 2. H. HYSLOP THOMSON.

Rehabilitation of Injured Air Crews

SIR,—I read with considerable interest Flight Lieutenant R. N. Houlding's article on the rehabilitation of injured air crews (September 27, p. 429), and while I congratulate him on the work that is being done, I do feel that he is missing quite a lot by not utilizing occupational therapy to a much greater extent. To quote from the article: "More improvement is made in the early stages of treatment by encouraging the patient to concentrate on overcoming his disability by working away at it all day long. In the later stages the patient's attention is diverted from his injured part by participation in competitive games."

I think here the author acknowledges that the patient's mind must be diverted from the injured part, and I am sure that the remedial measures adopted in the article do not do that. Even in the competitive games the patient's mind is still fixed on how much the injured limb or damaged joint will stand. The same is true of physiotherapy; the patient's whole attention is fixed on the injured part, whereas in occupational therapy his mind is guided away from his injuries by means of pleasurable occupations, constructive and absorbing, by no means boring or seemingly unnecessary, but actually with an additional educational value. And yet the very movements so necessary for rehabilitation are brought into repeated play in a way in which the patient is hardly conscious of the fact that they are being so used. In this way the patient reaches the same stage of rehabilitation, but reaches it by more pleasant pathways, and I am sure that by the addition of occupational therapy, properly employed by a qualified occupational therapist, to the means at the writer's disposal, he will be able to do away with the "notice" illustrated and quoted in full in the caption of Fig. 1.—I am, etc.,

ANDREW SHEPHERD,
Medical Superintendent of an E.M.S. Hospital with a Special Department for Orthopaedic Cases.

Sept. 27.

Treatment of Haemorrhagic Disease of the Newborn

SIR,—The article on the treatment of haemorrhagic disease of the newborn (September 27, p. 433) is interesting, and the subject is one concerning which I should like to hear more.

It has not been my lot to deal with many of these cases, but chance observation led me to the application of a simple method which has been successful in my past five cases. Very early I came to the belief that simple transfusion of blood was by no means a certain method of therapy. Some factor other than mere quantity of fresh blood was required. I turned to the injection of blood into the child's back, and this happening followed. In my first two cases I injected the mother's blood, but with no effect. The father was not available in the first case, but his brother was found and his blood injected. Recovery followed immediately. In the second case the father's blood was also got, with the same pleasant result. Since then I have had three cases, in each of which I have used the father's blood, and each one has recovered. In the two most recent ones, because they were severe, blood running from mouth and rectum, I have also used hemoplastin (P. D. and Co.).

The method I use is to take 2 c.c. of 4% citrate to 20 c.c. of the father's blood and inject this subcutaneously and intramuscularly from the shoulders to the buttocks of the child. I have seen no bad effects either locally or generally from so doing. At the same time I now give 2 c.c. hemoplastin intramuscularly into the thigh, and repeat this in twelve hours. Likewise I give from one to two drops of cod-liver oil in each of frequent small feeds.

I quote this method, not to detract from the value of vitamin K treatment, but merely to record a method that appears in a small number of cases to be giving consistent good results. I should very much appreciate the criticism of those with a much wider experience of the treatment of these cases than I possess. I intend to replace hemoplastin by vitamin K, but should I omit the father's blood?—I am, etc.,

Dundee, Sept. 29. JOHN J. ROBB.

Treatment of Impetigo

SIR,—I have followed with some interest recently the correspondence on the subject of the treatment of impetigo and scabies. During the last year I have been more than usually intimate with these two diseases, for I have been in charge of a reception station receiving such cases from at least a dozen different units spread about over an area of 400 square miles. Owing to the excellent sanitary and ablution arrangements (the building was erected to a pre-war reception station design) the treatment of the scabies patients, and the exceptionally satisfactory results obtained, cannot be fairly compared with what is possible in less well-equipped premises. Therefore I will confine these notes to the treatment of impetigo, for this can be carried out similarly in any normally equipped treatment centre.

The treatment, of course, varies with the widely different states of the patients on admission. It is noteworthy that very little attention has been paid to this polymorphism in the correspondence so far published. Roughly the impetigo cases may be grouped for treatment purposes as follows:

1. *Weeping Type.*—Large sero-rrhoeic areas, with perhaps a few isolated patches of scales, occurring on the neck, under the chin, on the face and ears (rarely on scalp and forehead), and usually associated with more or less thickening of the underlying corium with "bloated" appearance due to subacute inflammation.

2. *Encrusted Type.*—Dry, scaly, discrete, and itchy; chiefly on face, but, depending on severity, may extend on to the forehead, scalp, ears, and neck.

3. *Pustular.*—The secondarily infected type. Staphylococcal pustulation (Bockhart's impetigo) usually associated with dry encrusted type, and common after inefficient treatment; face, neck, and ears; often very resistant.

4. *Infiltrating Type.*—Corium infected: "ecthyma"; small areas usually on forehead or temporal regions, where burrowing infection has reached and penetrated the corium; often result of failure to receive early treatment, or of inadequate treatment of "encrusted" type.

5. *Fissured Type.*—Streptococcal fissures especially occurring at angles of the mouth ("perlèche") and behind and below auricles.

After much experimenting the principles I adopted were these: (*a*) First render the area entirely dry. (*b*) Remove crusts and scales only if this is possible without damaging the underlying epidermis. (*c*) Keep scalp clean by regular use of spirit soap. (*d*) Use suitable ointment, which must be massaged well into the affected areas with the finger-tips. (*e*) Use face-mask at night to prevent spread and contamination of healthy areas from pillow and fingers during sleep.

1. The weeping type needs to be rendered dry. I apply boric acid powder on lint directly to the sero-rrhoeic areas. If the powder is used freely enough there will be no adherence of the lint. These cases often show profuse subepidermal oedema, and the spread of infection reacts very favourably to M and B 696 2 grammes stat. and 1 gramme t.d.s. thereafter for two days. In about three days the areas are usually dry, the oedema has subsided, and the "creaking leather" feeling which the patient first noticed has disappeared. When hard crusts have formed and there is no further exudation I apply ung. hyd. nit. fort. night and morning, without removing the crusts, for two days. On the next day a compress of lint wrung out of hot 2% boric acid solution is applied to the whole crust-covered area, and repeated at intervals of fifteen minutes for one hour. The crusts dissolve away easily and a clean surface is left. An ointment ("two-in-one") made up of equal parts ung. hyd. nit. fort. and ung. zinci is then applied and well massaged into the skin for about ten minutes with the finger-tips by the patient himself under super-

vision. Thereafter this ointment is applied twice daily, and before the morning application the patient washes his hair, scalp, ears, face, and neck with spirit soap. After the evening application a face-mask is fitted (made of lint to cover the whole affected area). This routine is continued for three or four days, by which time the disease has usually disappeared. Occasionally, in very severe cases, the boric compresses have to be repeated about three days after the first application. The average time to cure these cases is eight to fourteen days.

2. The encrusted type (the average impetigo contagiosa of the textbooks) is already at the dry stage. The hair, scalp, ears, face, and neck are first washed with spirit soap and afterwards the "two-in-one" ointment is applied. This ointment is repeated at night as before. Most of the crusts are soaked off in the first wash with spirit soap, the remainder succumb to the second; on no account are any crusts "picked off." The complete routine is repeated daily and the patient is usually ready for discharge in seven to ten days.

3. In the pustular type the whole pustular area is first treated with the boric compress technique. Thereafter the "two-in-one" ointment is used as before (daily washing with spirit soap before the morning application). Usually one series of the boric compresses (over one hour) is sufficient; occasionally a second is required two or three days later. These cases are often resistant. They take about ten to fourteen days to clear.

4. The infiltrating type yields to hot boric compresses followed by application of tinct. benz. co. twice a day. The scabs must not be picked or scratched off, or the resulting scarring will be very unsightly, and also the infection will be encouraged to penetrate deeper.

5. The fissured type is often very resistant but decidedly less contagious than the other types. The fissures at the angles of the mouth usually yield to application of tinct. benz. co. and small strips of zinc plaster (about 1/4 inch wide and 3/4 inch long) placed vertically at the angles of the mouth to prevent stretching of the healing edges. The same applies to the ears.

It will be noticed that no mention has been made of shaving the head. The head is seldom affected initially, but becomes infected later on if treatment is not vigorous enough or if the patient twists a lot on his pillow at night without a mask over his face. I consider that it should never be necessary to shave the scalp. Occasionally it may become necessary to cut the hair moderately short (little more than the soldier's ordinary crop) for about 1½ inches above the ears and round the back of the neck. I have never yet found it necessary to shave the head. Spread to the scalp is prevented by the frequent washing with spirit soap, and the few isolated patches that may occur can be adequately dealt with, after the crusts have been softened and removed in the usual way, by the "two-in-one" ointment. The very resistant patches can be saturated by painting with 5% silver nitrate solution in meth. I find it a great incentive to conscientious self-treatment by the patient to tell him that if the disease spreads to his scalp it may be necessary to have his hair shaved away; this usually results in redoubled efforts to limit the course of the complaint. I make, too, a particular point of the ritual of washing with spirit soap. It is important that the hair shall be free from scurf and any form of irritation, as this is a potent source of infection through scratching fingers. Also it is important to see that the washing is done in order from the least affected to the most affected parts: not all areas at the same time, as there is then greater risk of carrying infection. Also the spirit soap stimulates keratosis, which hastens the desquamation of diseased cells.

The average time taken to cure all cases is in the neighbourhood of ten to fourteen days. Only very rare cases will take longer, and then only because the treatment is not vigorous enough, not conscientiously enough supervised, or because the patient is purposely retarding his progress (I had one such patient who was found to be removing the ointment as soon as it was applied, dabbed himself freely with a proprietary poison with a prodigious name, and complained that the irritation of his face was so intense that he could not bear to continue treatment; he wasted many valuable days having soothing lotions and ointments in consequence). I have heard of cases taking fifty and sixty days to cure—one champion brand of streptococci sustained a combined attack (so I am led to believe from the notes) for 108 days. Such cases have not come my way. I have heard of cases of the weeping type treated over a long period by *x* rays at weekly intervals: their improvement coincided with the intervals; others had been painted to resemble Early Britons by orderlies with artistic and possibly humorous tendencies; a few were part of a generalized sensitization dermatitis and were probably not impetiginous at all.

In conclusion it must be said that it is imperative that the nursing is of a high order. One must be sure that injunctions given to nursing orderlies are carried out to the letter. I was ably and faithfully assisted by a very conscientious team of orderlies, to whose efforts I attribute in very large part the excellent results obtained.—I am, etc.,

Sept. 28. JOHN W. W. JAY,
Captain R.A.M.C.

Technique of Relaxation

SIR,—As a psychotherapist, I agree more than heartily with Dr. W. Nunan's objection (September 20, p. 428) to "the airiness of the use, abuse, and ill use of the word 'relaxation' in the literature of psychotherapy." As he points out, telling a patient to relax is a most efficient way of making him self-conscious and tense. Direct suggestion is rarely, if ever, as effective as indirect implicit suggestion—certainly not so in inducing relaxation of mind or body.

A few practical pointers from long experience may help Dr. Nunan and others who want concrete advice. Much of the G.P.'s work is now concerned with "shell-shocked" men discharged from the Services; blitz-shocked and war-harassed and neurotic civilians generally. And relaxation induced by suggestion until it becomes a conditioned habit is about the simplest and most generally useful technique of minor psychotherapy for the G.P. (see Schultz's *Autogene Trainung*, Jacobsen, etc.).

Never use the word "relax"; suggestion should be implicit, not explicit.

Optimum conditions are: the patient lying on a couch, but an ordinary easy surgery chair is adequate and, better still, an old-fashioned straight-back with high-elbowed arms; a quiet room, and a natural chatty manner and voice on the part of the doctor; eschew the stage hypnotic voice or the monotonous repetitious sing-song that so many beginners affect—such hocus-pocus irritates, antagonizes, and arouses the suspicions of intelligent patients and confuses the dull ones. Walk about the room, do odd jobs, talk about other things, and even turn your back on him until he settles down. He will then not feel that he is being "influenced" or hypnotized, and any possible fear or distrust is disarmed; and don't be unctuous or over-persuasive.

My own technique varies but is often like this. At first let him sprawl in any position he finds comfortable. Then point out that every joint and limb has an optimum position which loosens the muscles most, and this varies with the patient and with his mood. Pick up his joints and adjust them in that position. The "healing hand" is a very real thing: the contact of one sympathetic human being with another has quite a magical effect which modern medicine need neither despise nor abuse. The patient's knees should be slightly everted and bent, or ankles crossed; palms loosely crossed or grasped across the abdomen or flexed by the side (some knowledge of surgical anatomy is helpful); head low on one cushion or none; or a neck pillow *à la Japonaise* and/or such pillows under the knees and small of the back, but this is an ultra-refinement hardly necessary.

Adjust, too, the neck and lumbar spine and facial muscles and tense mouth or eyes. Pick up the limbs and let them flop into the easiest position. Touch eyelids and forehead wrinkles and mouth, and very gently massage them into looseness with the balls of the fingers or thumbs. This causes the patient to look up and tires the ocular muscles into relaxation. I had a rather neutral Japanese kakemono picture on the otherwise blank wall facing him, to which his eyes would naturally stray; the design happened to be a greyish swirl of cloud or smoke which spiralled up to a point, and the rhythm and line of the picture seemed to lead the eyes irresistibly up to that point. Soon the eyes tire and tend to close. Then gently close the eyes and tell him to keep them shut if he feels like it. I have seen tense patients fall asleep, but this is no harm and means that the patient is certainly acquiring the technique.

Often I get him to cross palms on the abdomen, close his eyes and follow passively with his mind the rise and fall of the abdominal respiratory movements, without any attempt to con-

trol the breathing but merely to become increasingly aware of it. Let the emphasis be on expiration and the fall of the palms, because inspiration and breath-holding are normally conditioned and associated with effort, while expiration is associated with relaxation and sleep, and there is, I understand, a larger expiration/inspiration ratio during sleep and rest. Tirala's book on hyperpiesis and its relation to breathing is worth reading. So are the empirical yoga axioms and advice: yoga (not the fake stuff so over-written, but its classics as translated by Indians) can teach Western medicine something in this respect. But words are at best a poor means of conveying and teaching muscular and kinaesthetic skills.

The technique is not difficult for doctor or patient as a rule. Many patients pick it up after a few sessions of five to twenty minutes; others can never learn it, even with major psychotherapy. Once acquired, it can be practised at odd moments, before sleeping, on a bus, or (paradoxically enough) while working efficiently and without energy-wasting fuss. A common-sensical sympathetic doctor can, by trial-and-error practice, soon acquire a technique that will actually save his time and temper with neurotic tense patients. He may have the gratification of seeing his patients "snap into" the habit of relaxing, once for all time.

Relaxation is not a radical but a symptomatic technique of psychotherapy. None the less, it may help to break the vicious circle which all neurosis at rock-bottom is; I have found it useful even with psychotics. The only danger I know of is that the patient might with faulty technique become too attached to his—or her—doctor. But then a doctor who cannot keep the patient-doctor relationship under control is surely not a good doctor.—I am, etc.,

Bridge of Earn, Perth, Sept. 29. HENRY HARRIS, M.D., D.P.M.

Raspberry-leaf Extract

SIR,—When in general practice some years ago I had a patient whose first child was stillborn after a long labour. At 36 years she fell pregnant again. Believing that "raspberry tea" would influence her wish to have a daughter, she began at the third month to drink four pints daily of an infusion of raspberry leaves. The pulse rate rose from 86 to 106, and the blood pressure from 120/80 to 146/80 between the third and fourth months. Heart sounds were "pure"; there was no oedema; and the patient was active and well, although the rapid pulse and raised pressure persisted till term. Fourteen days past her time, after an easy labour of two hours, the baby (a girl) was born "in the caul."

Recent work on raspberry-leaf extract may explain some features of this case.—I am, etc.,

Worcester, Sept. 24. J. GRAHAM SCOTT, M.D.

SIR,—I am extremely interested in Sir Beckwith Whitehouse's publication (September 13, p. 370), as I have so far been unable to discover in our literature any explanation of the action of raspberry leaf on the uterus.

When I was in general practice in London I heard about it through a patient, and thought it worth while trying in the case of a multipara whose previous confinements had all been very difficult. To my surprise the woman had an easy time. As it seemed a harmless enough prescription, I ordered it subsequently for a routine measure in all confinements, especially in elderly primigravidae, where I became convinced of its usefulness for avoiding perineal tears. Although the labour pains seemed less severe in themselves, the actual time was rather shorter than usual, dilatation more complete, and puerperium uneventful. For a fortnight before the calculated date the mother would take a wineglassful of the tea t.d.s., and a pint of it as soon as the pains set in.

Sir Beckwith makes me feel that I need no longer consider myself a quack for using a remedy at which some of my colleagues used to smile tolerantly when I mentioned it.—I am, etc.,

Redruth, Sept. 25. W. E. R. MONS.

Thirst at Sea

SIR,—I wish to draw attention to the possibilities of ion exchange adsorbents in relation to the problem of obtaining a potable fluid from sea water.

The abstract (*Chem. and Ind.*, 1941, **60**, 378) of a paper by R. J. Myers *et al.* claims that water treated first by a cation exchange adsorbent (phenol-aldehyde resin) and then by an anion exchange adsorbent (amine-aldehyde resin) is freed from all dissolved salts. This method is proposed as a practicable means of removing salts from various types of solution. Sea water, though not specifically mentioned, would apparently come within the scope of the claims made, and the possibility of devising equipment suitable for use in ships' boats might usefully be examined. The materials necessary for regenerating the adsorbents are presumably strong acids and alkalis. These are inexpensive and can be carried in concentrated form.

I have found that zeolite of a type commonly used in domestic water softeners can be charged with silver ions, and that the product, shaken with 3% sodium chloride solution, yields pure water on filtration. By this device Dr. Hardy's objection (August 23, p. 286) to Sir Leonard Rogers's suggestion (August 9, p. 211) for the use of silver salts is avoided. The method would probably be impracticable at sea for various reasons connected with the high atomic weight of silver and mechanical clogging of the adsorbent by insoluble silver chloride. The idea might, however, be valuable in the laboratory as a means of removing soluble chlorides from some solutions.—I am, etc.,

Glaxo Laboratories, Greenford, Sept. 29. W. J. HURRAN.

A Plea for Flexibility

SIR,—I write to inform your readers of an incident which illustrates a rather obvious, and surely remediable, discrepancy between the Army and the civilian medical services.

On the evening of a day filled with the usual daily struggle to keep abreast of the rapidly rising surgical waiting list, and during twelve hours of which six emergencies had already been admitted —50% being due to various navigational blunders on the part of military drivers—on this evening, at 9.30 o'clock, a telephone call from a large military hospital twenty miles away informs us that a N.A.A.F.I. worker has developed acute appendicitis. Further conversation on the telephone establishes the fact that, whereas the military hospital has plenty of beds, we have already filled the last bed even in the ophthalmic ward with a surgical case. Yet, in spite of this, and the fact that the patient is an acute surgical emergency, he must travel those twenty miles, to be put into a made-up bed, and to be operated upon by a tired surgeon.

In contrast with the above incident, I would like to point out that, although as a general rule we do not treat military patients at this hospital, in the event of an urgent military case being brought into our emergency ward that case is treated here until he is deemed fit for removal to a military or E.M.S. hospital. Must a little latitude of arrangement such as this in the saving of human life remain impossible in the R.A.M.C.?—I am, etc.,

Sept. 22. "R.S.O."

RADIOLOGICAL HOUSE-SURGEONS IN THE E.M.S.

Hospitals are requested to bring the following information to the notice of their medical officers as soon as possible: (1) The Ministry of Health is prepared to enrol in the Emergency Medical Service radiology house-surgeons at selected hospitals in London and the Provinces. (2) Applicants must satisfy the deans of their medical faculties or schools that they intend to take up radiology and are prepared to enter for a diploma in medical radiology at the end of their course of study. The selected hospitals will be so situated that attendance at courses of instruction will be practicable, and successful applicants will be required to undergo the appropriate course of instruction, paying the necessary fees. Applicants must have held a house appointment at a hospital for at least six months, and preference will be given to those with longer clinical experience. (3) The salary will be at the rate of £200 a year, with an additional £100 for board and lodging if the officer is required to live outside the hospital. (4) Applications should be made as soon as possible to the Director of Establishments, Ministry of Health, Caxton House, Tothill Street, S.W.1, through deans of medical faculties or schools, or through regional hospital officers or group officers (London sectors).

Obituary

Dr. Charles Leonard Digby Roberts, who remained in Guernsey to tend the needs of the civilian sick during the period of German occupation, died at St. Peter Port on April 21 soon after undergoing a major operation. He was born at Exmouth in 1882 and graduated M.B., Ch.B. at Edinburgh University in 1908. From there he proceeded to London to study for the English Fellowship at St. Bartholomew's Hospital. He passed the Primary Examination but became interested in tropical medicine and went out to India, where he spent the greater part of his professional life. In due course he took the D.T.M.&H. from the London School of Tropical Diseases and became a Fellow of the Royal Society of Tropical Medicine. For some years he was medical officer of the Charteris Hospital in Kalimpong, a remote outpost, chiefly noted as being the railhead for numerous Mount Everest Expeditions. After the outbreak of the war of 1914-18 he joined the I.M.S., seeing service in the Waziristan and Persian Gulf campaigns. After the war he practised for a short time in Darjeeling, and then went to Assam, where he was medical officer to the Mariana Tea Association for many years. Finally he retired from India and began practice in Guernsey, where he had hoped to retire and enjoy a well-earned rest. He was an active member of the B.M.A., and had been honorary secretary of the Assam Branch and chairman of the Guernsey and Alderney Division. His chief hobby was the study of natural history: butterflies, birds, flowers, trees, sea shells, and freshwater shells. In India he amassed a very fine collection of butterflies, and some of his specimens proved to be new discoveries and are preserved in the Natural History Museum in South Kensington and in Bombay. His knowledge of the flora of the Channel Isles was a source of wonder to those who accompanied him on his energetic walks along the cliffs and country lanes which were so dear to him. Dr. Roberts is survived by his wife, daughter, and three sons. The sympathy of all will go out to Mrs. Roberts in her lonely exile.

Dr. Matthew Bruce died on September 20 at the age of 85. After graduating M.B., C.M. of the University of Edinburgh in 1885 he practised at Ashington, Northumberland, for half a century, and held the posts of medical officer of health, public assistance medical officer, and public vaccinator for many years. A past chairman of the Morpeth Division of the B.M.A., he was a regular attendant at Annual Meetings of the Association. He was keenly interested in first aid and home nursing, and lectured on these subjects over a long period. In spite of his advanced age he was actively in charge of a first-aid post until the day of his death. In the words of the honorary secretary of the Morpeth Division, "Dr. Matthew Bruce was liked by all his colleagues, and his bearded erect figure, always on a push cycle, will be missed by all who knew him."

Dr. Robert Hamilton of Harrogate died on September 24 at the age of 63 as the result of a street accident at Beverley, where he was acting as wartime deputy for a local practitioner. Dr. Hamilton was the son of a Bradford medical man, and from Bradford Grammar School went to study medicine at the University of Edinburgh, graduating M.B., Ch.B. in 1901 and proceeding M.D. in 1909. He was for some years a member of the Colonial Medical Service, and in the last war served in the R.A.M.C. with the rank of captain, afterwards practising in Oxfordshire and Somerset before his retirement to Harrogate in 1935.

I read with great regret of the death of Dr. William Robertson (writes Mr. Lewis G. Cruickshank, F.R.C.S.). I had the privilege of studying under his guidance both as an undergraduate and later during the D.P.H. course. He was a fine teacher, and his long experience in the Public Health Service made him an excellent exponent of the practical problems of the service. He was a most approachable man, and always ready to discuss with his students the problem of their future career: he was much interested in medical education, and contributed articles on the subject of postgraduate study to the *Surgeon's Hall Journal*. His passing will be mourned by many, and the loss to the Edinburgh School of Medicine is a great one, for he was a universal favourite with students and staff alike.

The following well-known foreign medical men have died: Prof. Anton Waldmann, head of the sanitary department of the German War Office, as the result of a motor-car accident last autumn, aged 63; Dr. Anton Henrichsen, director of the cantonal sanatorium at Herisau, best known as the author of poems and plays under the pseudonym of Otto Hinnerk; Dr. Walter Vogt, professor of anatomy at Zurich, aged 53; and Dr. Albert Kocher, a Berne surgeon, aged 45.

Medical Notes in Parliament

Lord Dawson on the Food Value of Eggs

In the House of Lords on September 30 Lord Dawson spoke in a debate on livestock and feeding-stuffs. He laid particular emphasis on the nutritive value of the egg, and, making a comparison with milk, said that the egg was rich in protein and vitamins and, so far as vitamin C was concerned, it was even better than milk. Together, milk and eggs were a tower of nutritional strength. The egg was a very digestible and easily handled food. All authorities were agreed that without eggs and milk they could not make light food, which was especially important to workers who were beginning to get weary in mind and weak in their digestions. Although it was right that there should be a priority of eggs for children and some invalids from the point of view of preventive medicine, from the point of view of keeping the active population well and fit they could not neglect the fact that the availability of eggs played an important part. He hoped the Minister of Food would take no steps to ration eggs further, but would leave this matter to localities to be dealt with by voluntary efforts. The localities should look after the egg needs of the children and ailing citizens, and as for the rest the requirements might be met by means of a pool. The health of the workers must be maintained on a high level.

Turning to the home production of eggs, Lord Dawson said that it was going down by about 20% per hen. We could produce protein-rich foods suitable for our animals within the next two or three months. In the manufacture of acetone there was a by-product containing 50% of protein which was quite suitable for feeding poultry and animals. Castor-bean meal, now used as a fertilizer, contained an ingredient poisonous to animals, but by the ingenuity of our chemists this ingredient could be removed quite satisfactorily, leaving a protein-rich food available for animal feeding. A synthesized vegetable protein of high value had been discovered recently. It was made in part from yeast, and, he believed, was suitable for mass production. Could not large-scale production be expedited? There was even a prospect of the product being cheap, and it was going to be available for human beings. Experiments had shown that this added to the value of bread, and was extraordinarily good in the nourishment of children. Here was a product which would not only help human beings but would help in the protein feeding of animals. He urged the Minister of Food to hustle this thing on.

In conclusion, Lord Dawson appealed to the Government to postpone the reduction of poultry rations to one-sixth for a few weeks, in order to give a little more time. He said that the reduction of two-thirds which had already taken place was too great, and he did not want to see the poultry industry damaged beyond all recovery. The order which had been issued for the reduction of sales of tuberculin-tested milk by more than one-third by October 18 was a mistake, and it should be put right.

Defective Hearing in the Army

On September 30 Captain Margesson told Sir Francis Fremantle that he had no information about how many men and women had been invalided out of the Army or incapacitated on account of defective hearing. Sir Francis Fremantle asked Captain Margesson to consider giving some instruction whereby men invalided out of the Army for deafness might be passed on

to the National Institute for the Deaf in order that good use might be made of these men, many of whom were extremely valuable although no longer of use for military service.

Food-poisoning on Board Ship

On September 30 Dr. MORGAN asked the Minister of Health whether, during 1938, 1939, and 1940, there were any further outbreaks of food-poisoning on board ships; whether any further outbreaks of toxic peripheral neuritis, similar to the outbreaks of Ginger or Jake paralysis in the United States, were observed and recorded; whether the fine medical work in this connexion of the medical officers of his Ministry, reported in the 1938 Annual Report of the Ministry's chief medical officer, had been repeated; whether special watch had since been kept for such outbreaks; and whether appropriate commendation had been made to the officers concerned. Mr. ERNEST BROWN said that no further outbreak of toxic polyneuritis or of other serious food-poisoning on board ship had come to his notice. He greatly appreciated Dr. Morgan's tribute to the work of his medical officers, and assured him that their watch for any serious outbreak of the kind to which he referred was a close one.

Employment of Alien Doctors

Miss RATHBONE asserted on October 2 that many general practitioners, especially in neutral and reception areas, were seriously overworked owing to the calling up of their medical colleagues, yet were debarred from securing the assistance of alien doctors in their private practices. She asked Mr. Ernest Brown to change the Regulations to permit alien doctors, accepted for the War Emergency Register, to engage in private practice under conditions thought necessary to protect British doctors, such as the limitation of the permit to the duration of the war, and, if necessary, the restriction of the permit to doctors required to work as assistants to, or partners of, British doctors. Mr. BROWN replied that under a recent Order an alien doctor who fulfilled the other necessary conditions could be placed temporarily on the *Medical Register* if he was to be employed as an assistant to a British doctor in private practice. The employment was in each case subject to the approval of the Home Secretary. A practitioner who desired to secure the services of an alien doctor could take the normal steps available to the profession, or, if in doubt, could write to the Ministry of Health.

Sir FRANCIS FREMANTLE remarked that the Central Medical War Committee would undertake these arrangements.

Medical Personnel Priority Committee

In a reply on October 2 to Sir Francis Fremantle, Mr. ERNEST BROWN said an interim report had been received from the committee presided over by the Under-Secretary of State for Dominion Affairs on the distribution of medical man-power. Action was being taken on the recommendations. These included suggestions for the establishment of regional committees to promote the maximum co-operation between civil and Service medical establishments, the continued recruitment for the time being of medical officers for the Forces at the present rate, the compilation of particulars of bed accommodation and staffing for all civil hospitals, and measures to secure greater mobility of resident medical staffs between one hospital and another.

Tuberculosis Increase: Special Inquiry

Dr. SUMMERSKILL inquired on October 2 to what cause Mr. Ernest Brown attributed the increase in tuberculosis. Mr. BROWN said he had arranged for a special inquiry, with the assistance of the Medical Research Council, into the causes of the wartime increase in tuberculosis. On June 30 last there were 1,763 persons in England and Wales who had been for upwards of ten days on local authority waiting lists for institutional treatment. Information was not available on the incidence of non-pulmonary tuberculosis in areas where pasteurized milk was unobtainable. The Ministry of Health was arranging to make available some E.M.S. beds.

Medical Examination of Miners.—On September 30 Mr. GRENFELL informed Miss Ward that to secure uniformity and speed in the urgently needed return of men to the pits under the registration scheme, the question of medical examination was determined in each case by officers of the Ministry of Labour and National Service on the facts brought to their notice at the interview.

The Services

NAVAL AWARD

Surgeon Commander George McCoull, R.N.V.R., and Acting Surgeon Commander Gerald Frederick Stavely Parker, R.N.V.R., have been awarded the Royal Naval Volunteer Reserve Officers' Decoration.

CASUALTIES IN THE MEDICAL SERVICES

ROYAL NAVY

Surgeon Lieut.-Commander CLAUD DENIS DELACOUR DE LABILLIERE, R.N., who was recorded as "Missing" in the *Journal* of June 21, is now posted as "Missing, Presumed Killed" in an Admiralty Casualty List published on October 1. He was serving in H.M.S. *Fiji*, which was sunk in the operations off Crete in May last. Qualifying M.R.C.S., L.R.C.P. in 1929, he entered the Royal Navy as surgeon lieutenant in the following year, and was promoted to surgeon lieutenant-commander in 1936. He had been a member of the British Medical Association since 1931.

ROYAL ARMY MEDICAL CORPS

Prisoners of War

Temporary Major Robert Harvey.
Temporary Major Patrick David Clifford Kinmont.
Temporary Major George Albert William Neill.
Captain Arthur Geoffrey Veasey Aldridge.
War Substantive Captain Charles Alan Hutt.
War Substantive Captain David Frew Wood.
Lieut. James Manson Knight.

DEATHS IN THE SERVICES

Lieut.-Colonel HENRY GEORGE LUTHER WORTABET, I.M.S. (ret.), died at Bournemouth on September 19, aged 88. He was born in Syria on September 5, 1853, and was educated at the University of Edinburgh, where he graduated M.B., C.M. in 1878, proceeding M.D. in 1883. Entering the I.M.S. as surgeon in 1879, he became lieutenant-colonel after twenty years' service, and retired in 1909. He served in Afghanistan in 1880, receiving the medal, and in the Burmese campaigns in 1886-8, taking part in the operations of the 4th and 6th Brigades, and gaining the Frontier medal with two clasps. He had been a member of the British Medical Association for fifty years.

Medical News

The activities of the Royal Medical Society of Edinburgh are proceeding as usual, though the war has necessitated the temporary abandonment of the annual dinner. The inaugural address for the forthcoming session will be delivered by Surgeon Rear-Admiral Sir W. I. de Courcy Wheeler on Friday, October 17, at 8 p.m. in the Hall of the Society. The title is to be "What Society has Gained by the Progress of Surgery." During the session addresses will be given by Colonel F. A. E. Crew, Prof. G. B. Fleming, Prof. A. T. Jurasz, Dr. J. Trueta, and Prof. Samson Wright.

The 1941 annual meeting of the National Society for the Prevention of Blindness (U.S.A.) will be held in New York City from December 4 to 6.

The Duchess of Portland has accepted the presidency of the London Ambulance Benevolent Fund. Founded less than three months ago, the Fund has already raised £2,500, and has been the means of help in over forty cases of distress among members of the regular and auxiliary Ambulance Service and their dependants.

Mr. Geoffrey Williams Carte, F.R.C.S., surgeon, London, has been commended for brave conduct in civil defence.

On September 11 the New Zealand House of Representatives passed the Crimes Amendment Act, substituting life imprisonment for the death penalty for murder and abolishing flogging.

Dr. H. D. Clementi-Smith has been elected a Warden of the Mercers' Company, the first, in order of civic precedence, of the twelve great Guilds of London.

The Department of Health of the City of New York is planning to establish an Institute of Scientific Research.

No. 38

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended September 20.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for : (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for : (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases ; a blank space denotes disease not notifiable or no return available.

Disease	1941 (a)	(b)	(c)	(d)	(e)	1940 (Corresponding Week) (a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	121	4	34	4	5	119	9	33	—	6
Deaths		—	1				1	1		
Diphtheria	957	40	237	15	19	1,058	38	370	24	41
Deaths	23	1	7	2	—	37	1	10	2	5
Dysentery	102	9	68		—	46	1	57	—	1
Deaths		1	—	—	—			—	—	—
Encephalitis lethargica, acute	6	—	—		—	6	1	1		—
Deaths		—	—				1	—		
Enteric (typhoid) fever*	27	1	4	10	4	68	2	18	4	1
Deaths	—	—	—	—	1	1	—	—	1	—
Erysipelas		—	45	7	3		15	45	7	2
Deaths		—	—				1	—		
Infective enteritis or diarrhoea under 2 years										
Deaths	38	1	13	17	11	45	4	25	21	13
Measles	612	18	14	23	—	7,435	120	445		8
Deaths	1	—	—	—	—	9	2	4	—	—
Ophthalmia neonatorum	76	3	7		—	68	4	18		—
Deaths										
Paratyphoid A and B	125	6	11							
Deaths	—	—	—							
Pneumonia, influenzal†	434	15	2		—	465	20	2		1
Deaths (from influenza)	8	—	—	—	1	7	1	3	—	1
Pneumonia, primary			140	3				104	3	
Deaths				4	2				4	5
Polio-encephalitis, acute	3	—				2	—			
Deaths		—					—			
Poliomyelitis, acute	28	1	8	3	1	38	—	4	—	—
Deaths		—	—				—	—		
Puerperal fever	—	4	14	3	—	4	4	11	1	—
Deaths										
Puerperal pyrexia	134	4	15		3	119	7	17		1
Deaths										
Relapsing fever	1	—			—	—	—			—
Deaths										
Scarlet fever	1,140	34	195	48	22	1,538	71	238	23	47
Deaths	1	—	—	—	—	1	—	1	—	—
Small-pox	—	—	—		—	—	—	—		—
Deaths	—	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths			—	—	—			—	—	—
Whooping-cough	2,289	196	106	45	30	1,245	9	67		18
Deaths	14	1	2	2	—	6	—	1	2	1
Deaths (0–1 year)	272	19	69	25	19	290	38	73	29	29
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	3,429	427	512	164	94	5,871	1,763	564	179	150
Annual death rate (per 1,000 persons living)			11·2	10·9	‡			11·4	14·0	13·1
Live births	5,079	460	812	374	172	5,945	772	763	291	234
Annual rate per 1,000 persons living			16·5	24·8	‡			15·4	19·4	20·4
Stillbirths	170	14	37			227	25	41		
Rate per 1,000 total births (including stillborn)			44					51		

* Includes paratyphoid A and B for Northern Ireland.

† Includes primary form in figures for England and Wales, London (administrative county), and Northern Ireland.

‡ Owing to evacuation schemes and other movements of population, the birth and death rates for Northern Ireland are no longer available.

EPIDEMIOLOGICAL NOTES

Discussion of Table

In England and Wales the recent decrease in the incidence of measles and whooping-cough and the increase in the incidence of scarlet fever and diphtheria were continued in the week under review. In Scotland scarlet fever was the only one of these diseases which showed an increase compared with the preceding week. A large relative decrease of 25% (196 cases) was recorded in the notifications of measles in England and Wales. This rapid rate of decline has been a feature of the trend of measles during the past sixteen weeks. The total cases of measles recorded in the last four-week periods were 40,656, 19,916, 8,743, and 3,478, showing rates of decline of 50, 56, and 60% on the preceding monthly totals. The number of cases of measles notified during the week reviewed was one-twelfth of that recorded in the corresponding week of last year.

The number of notifications of whooping-cough in England and Wales was 421 less than in the previous week. This was the third consecutive week that a decrease has been recorded, the rates of decline being 4.5, 10.5, and 15.5%. In Scotland a decrease of 47 in the number of cases of whooping-cough occurred. The experience of Glasgow (67 cases out of a total of 106) still dominates the returns for this country.

The rising trend of the notifications of diphtheria in England and Wales resulted in an increase of 40 on the total of the previous week. A decrease of 17 was recorded in Scotland, following four consecutive increases. A small increase (10 cases) was recorded in the notifications of scarlet fever in Scotland for the ninth consecutive week. In England and Wales an increase of 135 was notified. The incidence of paratyphoid and typhoid diminished, and the total cases were the smallest number recorded since the first week of July.

Cerebrospinal Fever

With the exception of an increase of 10 cases in Warwickshire and 5 cases in Middlesex, the notifications of cerebrospinal fever in England and Wales, which exceeded last week's total by 3, did not show any special difference from the previous week's distribution. In Scotland a relatively large increase, from 23 to 34 cases, occurred. The increase was due to outbreaks in the counties of Angus, Fife, and Midlothian. Slightly more than half the total was contributed by the cities of Glasgow 12, Edinburgh 4, and Dundee 2 cases.

Dysentery

The slight increase of 8 was recorded in the notifications of dysentery in England and Wales. Small local outbreaks occurred in Shropshire (Wem R.D. 12); Cornwall (Bodmin M.B. 8); Warwickshire (Rugby M.B. 8); Yorkshire, West Riding (Halifax M.B. 6 and Brighouse M.B. 6). In Scotland, where the notifications exceeded last week's total by 1, the chief outbreaks were those of Dundee 19, Glasgow 10, Lanark County 10, and Edinburgh 6.

Poliomyelitis

Twenty-eight cases of poliomyelitis were notified in England and Wales, a decrease of 25% on the total of the previous week. The chief centres of infection were Middlesex with 5 (Edmonton M.B. 2), and Oxfordshire with 4 cases, which were all notified in Oxford C.B. In Buckinghamshire, where the most serious of the recent local outbreaks occurred, 2 cases were reported after an interval of a week without one. Both these cases were notified in Slough M.B., and this area had 4 cases during the week ending August 23. Two cases each were notified in the counties of Cornwall, Devonshire, Hampshire, and Surrey. Eight cases, compared with 2 in the preceding week, were notified in Scotland. Glasgow, with 4, was the only area with multiple notifications.

Week ending September 27

Cases notified in England and Wales during the week were: scarlet fever 1,258, whooping-cough 2,247, diphtheria 1,066, measles 745, cerebrospinal fever 94, acute poliomyelitis 38, dysentery 89, paratyphoid 100, typhoid 32.

Universities and Colleges

UNIVERSITY OF SHEFFIELD

The following candidates have been approved at the examination indicated:

Final M.B., Ch.B.—*Parts II and III:* H. Barrada, Pauline M. Hardcastle, L. Ishak, L. F. Q. Maclaine, Margaret E. Withers.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

Arnott and Erasmus Wilson demonstrations and Museum lecture-demonstrations will be given at the College (Lincoln's Inn Fields, W.C.) as follows: October 13, Prof. A. J. E. Cave, the constitution of the skull; October 14, Mr. L. E. C. Norbury, benign neoplasms of the rectum; October 15, Prof. Cave, vascular arrangements of the head and neck; October 16, Mr. Norbury, malignant neoplasms of the rectum; October 17, Prof. Cave, lymphatics of the head and neck; October 20, Prof. Cave, surgical anatomy of the nasal fossa; October 21, Mr. R. Davies-Colley, diseases of the testicle; October 22, Prof. Cave, surgical anatomy of the mouth and jaws; Oct. 23, Mr. C. E. Shattock, tumours of the kidneys; October 24, Prof. Cave, surgical anatomy of the pharynx and larynx; October 27, Prof. Cave, surgical anatomy of the liver and bile ducts; October 28, Mr. Davies-Colley, tumours of the intestines; October 29, Prof. Cave, surgical anatomy of the kidney and ureter; October 30, Mr. Shattock, tumours of bone; October 31, Prof. Cave, surgical anatomy of certain nerves. All the demonstrations begin at 2.30 p.m., and are open to advanced students and medical practitioners.

Letters, Notes, and Answers

All communications in regard to editorial business should be addressed to The EDITOR, British Medical Journal, B.M.A. House, Tavistock Square, W.C.1.

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Telephone No.—B.M.A. and *B.M.J.*: EUSTON 2111.

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QUERIES AND ANSWERS

Cancer in the Lower Animals

J. T. M. writes: I shall be glad if anyone can tell me what is the incidence of cancer among domesticated animals, particularly the cow, sheep, poultry; and fish. I have been told by an authority that cancer is rather common in poultry, affecting particularly their sexual organs.

Behaviour of Children and Adults under War Conditions

Miss Evelyn Fox, C.B.E., honorary secretary of the Mental Health Emergency Committee (24, Buckingham Palace Road, S.W.1), writes: This committee has been making an inquiry into the behaviour of children and adults under war conditions. Questionaries have been sent out to child guidance clinics, mental treatment clinics, psychiatric wards of emergency hospitals, and to psychiatric social workers in the reception areas. This inquiry was intended to be only a preliminary survey, and before proceeding further the committee would be very interested to learn whether any similar investigations are being carried out, either by groups or by individuals, and if so would welcome opportunities of co-operation.

Income Tax

Expenditure on Books

"X. Y." refers to an answer in our issue of July 16, 1941, and asks for a note on the decision in Simpson *v.* Tate.

*** The answer referred to was given on the understanding that the inquirer was in general practice and assessed under Schedule D; salaries, etc., are assessable under Schedule E, and the rule in that Schedule with regard to expenses is more stringent than the corresponding Schedule D rule. Dr. Tate was a county M.O.H. and claimed to deduct subscriptions to certain professional societies. In his judgment Rowlatt J. said that "taking in professional literature and all that sort of expense which enables a man to keep himself fit for what he is doing are things which can none of them be allowed." This decision seems to cover the purchase of books if the income is assessable under Schedule E.

LETTERS, NOTES, ETC.

Irrigation in Treatment of Diverticulosis

Dr. Bernard Myers (London, W.1) writes: Diverticulosis is not an infrequent condition in older adults, not difficult to diagnose from the train of symptoms and confirmation by *x* rays. Not only constipation but the tendency to attacks of diverticulitis with the accompanying discomfort and pain is apt to cause depression, especially in the more severe cases. From my experience of these cases I suggest that the essentials of treatment are a non-irritating diet free from pips, skins of fruit, or other indigestible material, the daily taking of liquid paraffin in sufficient but not in excessive doses, and irrigation of the colon from time to time. Cases that receive this treatment have, I suggest, not at all a bad time, and can enjoy life reasonably and play games. With regard to liquid paraffin, I find cases differ to some extent, but, generally speaking, a tablespoonful thrice daily suits many sufferers; but to some this would be excessive, and less must be taken, as too much causes too frequent action of the bowels with much discomfort and accidents in clothes. Others need more, and I know of a well-marked case in a man over 60, who takes two tablespoonfuls every morning before breakfast and the same quantity before the evening meal, and keeps free now from attacks of diverticulitis provided his colon is irrigated at least every two months. Irrigation must be done only by real experts, as those not properly initiated into the method may cause great discomfort or even danger. I believe that many bad cases need irrigation once a month and possibly more often. When it is properly done the patient complains of no pain or discomfort, but, on the other hand, a feeling of great relief and well-being. It is surprising to see the material removed from a diverticulum after a careful irrigation. Sufferers from diverticulosis should not strain at stool; indeed, there should be no need if the dose of paraffin be well regulated.

The Blunt Needle

Mr. A. P. Bertwistle, F.R.C.S.Ed. (London) writes: A blunt needle is at once a source of annoyance and danger. The chief danger is that the needle may break in the tissues, requiring operative removal. A second danger is that it must pass through the tissues more like a saw than a knife. If the needle is obviously rusty micro-organisms may lodge in the crevices untouched by antiseptics, save those of low surface tension, though not by boiling, of course. Hypodermic needles are now made of stainless steel; they become blunt very often by the tip bending backwards, usually over the lumen, and also from excessive use. They can be sharpened with the aid of an oil-stone. Gone are the days when a matchbox was, surreptitiously, used for removing rust. With regard to suture needles, I have the authority of Messrs. Thackray for stating that stainless steel has so far proved unsatisfactory, since it will not harden or temper as well as carbon steel. (In the present emergency they have been asked not to draw on supplies available.) Prof. John Hilton in a broadcast said that safety-razor blades became blunt as the result of an invisible rust forming on the cutting edge, it being impossible to dry the edge perfectly with a towel. If, however, the blade is finally cleaned with a rag moistened with a thin cycle oil it will keep its edge twice as long. Applying this principle to suture needles, if the needle be drawn through a piece of chamois leather impregnated with thin oil several times after use it will be found that the needle keeps sharp much longer, a point of value in these hard times.

Disclaimer

Drs. J. Robinson and M. Stock write from Manchester: Our attention has been called to a recent newspaper article concerning the treatment of influenza and colds in which our names appeared. We desire to state clearly that we have given no interview to the writer of the article or any other person, and that we had no knowledge of its proposed preparation or publication. We desire further to state that we take no responsibility for the nature or accuracy of the statements made or the facts alleged.

Corrigendum

In the report supplied to us of the meeting of the Association of Clinical Pathologists held at Cambridge on July 19 and published in the *Journal* of August 30 (p. 315) Dr. S. C. Dyke is recorded as having made observations on eosinophilia in glandular fever. Dr. Dyke was in fact discussing trichiniasis and not glandular fever, and he asks that this correction may be notified to our readers.